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PHYSIOLOGIC STUDIES ON THE STOMACH OF A WOMAN WITH A GASTRIC FISTULA

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ST. LOUIS

THE CHAIN of circumstances which permits direct observation and study of the interior of the human stomach is rare. In the entire record of medical history it has occurred but four times: (1) in Beaumont's classic study of Alexis St. Martin, first published in 1833,¹ (2) in Richet's study of a patient in 1878,² (3) in Carlson's study of Mr. V. in 1912³ and (4) in Wolf and Wolff's study of Tom in 1940⁴. Each of these was made on a male patient.

When the opportunity presented itself to study a patient who had undergone a gastrostomy, we considered it to be of value to add further observations to those which have been made, particularly since our patient was a young woman. The possibility that physiologic activity in the stomach of the female may differ from that observed in the male was suggested by the strikingly greater incidence of duodenal and gastric ulcer (a 4 to 1 ratio) reported for males.

REPORT OF A CASE

History.—On the night of Dec. 15, 1944, Doris B., a 21 year old Negro woman, while home for the Christmas vacation from college went to the medicine cabinet in the kitchen of her home to obtain some powders which she had been

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1. Beaumont, W.: Experiments and Observations on the Gastric Juice and the Physiology of Digestion, Plattsburgh, F. P. Allen, 1833, pp. 1-260.

2. Richet, C.: Du sac gastrique chez l'homme et les animaux, ses propriétés chimiques et physiologiques: Appendice A.: Tour de l'anatomie et de la physiologie, Paris, Germer-Baillière & Cie, 1878, vol. 14, p. 170.

3. Carlson, A. J.: Contributions to the Physiology of the Stomach: I., Am. J. Physiol. 31:151-168, 1912.

4. Wolf, S., and Wolff, G.: Human Gastric Function, New York, Oxford University Press, 1943, pp. 1-185.

in the habit of taking for dysmenorrhea. These consisted of a teaspoon of powder with several crushed acetylsalicylic acid tablets. Because of confusion in the placing of bottles in the medicine cabinet, she inadvertently took lye. She immediately complained of burning in the mouth, but this was soon replaced by a sensation of generalized pain which was constant in character and later was associated with vomiting.

The patient entered the Homer G. Phillips Hospital on Dec. 16, 1944, but on the request of her mother she was sent to St. Mary's Hospital, where emergency treatment was carried out and where she remained for sixteen days. Dysphagia constantly increased during this time. On Jan. 15, 1945, the patient was again admitted to the Homer G. Phillips Hospital, and five days later a gastrostomy was performed under spinal anesthesia. At that time a string was passed through the esophagus and dilation was carried out. However, the patient remained unable to swallow. Moreover, it was necessary to perform another gastrostomy on March 26 because of stenosis of the original opening. After this operation, the wound became infected and broke down, which resulted eventually in a large opening

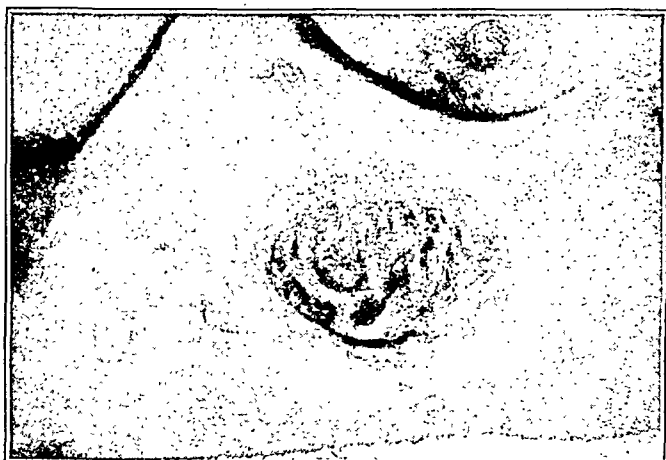


Fig. 1.—The cannula has been removed from the gastrostomy opening, with the patient in the erect position. The herniated mucosa is the posterior wall of the stomach and is the area where color changes were observed.

approximately 6 cm. in diameter lateral to the left rectus muscle. It was so large that feedings and gastric secretions were not retained but escaped; this led to excoriation of the skin. The patient lost considerable weight, and a specially designed soft rubber cannula was finally inserted in the gastrostomy opening to prevent leakage of gastric juice. A high protein liquid diet was given through the opening, and normal weight was soon regained.

Removal of the cannula revealed herniation of a considerable area of the posterior wall of the stomach through the gastrostomy opening, with increase in the intra-abdominal pressure (fig. 1). The gastrostomy opening was located along the anterior portion of the greater curvature of the stomach approximately 6 inches (15 cm.) from the pylorus and 7 inches (18 cm.) from the cardia. The external opening was lateral to the umbilicus and approximately in the mammary line. When the patient lay on her left side, the stomach emptied itself of its fluid content fairly well. The fluids can be easily collected in any glass vessel with a slight flare to the upper rim.

The size of the opening in our patient was 6 by 8 cm. Beaumont's Alexis St. Martin had an opening 6 cm. in circumference approximately 7 cm. to the left of the cardia near the left superior termination of the greater curvature.¹ Carlson's Mr. V. had an opening on the lesser curvature about 8 cm. above the umbilicus and a little to the left of the median line. The fistula was only large enough to admit a rubber tube 1 cm. in diameter, which was always kept in place³. Wolf and Wolff's Tom had a defect in the abdominal wall 3.5 cm. in diameter through which a collar of gastric mucosa herniated⁴.

The patient's personal history was not particularly unusual. Two brothers, the father, the mother and the stepfather are all living and well. Her menstrual history was not unusual except for moderate dysmenorrhea and slight menstrual irregularity during the early stages of her illness. Her friendships, likes and dislikes seem to have followed a usual pattern.

The patient had attended public school and high school and had been a year and a half at college. Her desire was to be a physical education teacher in an elementary school. Her scholastic standing was consistently above average, and she was the school's ping-pong champion. She stated that most of her desires and wants have been fulfilled without difficulty. On the basis of this history and after a rather long evaluation of her condition in Barnes Hospital, to which she had been transferred for further care, there was little evidence to substantiate any belief that the swallowing of the lye was other than accidental or that there was any intent to commit suicide.

Since it was believed that the patient presented such an excellent opportunity for physiologic study, she was approached with the request that she permit us to make observations on her stomach while she was undergoing other treatment. To this she readily assented with a definite show of enthusiasm at being able to perform something beneficial. These negotiations were carried out in a frank manner, with full explanations as to what was desired and what was planned and with the proviso, of course, that the plan for her treatment would not be interfered with and that injurious studies would not be undertaken.

Methods.—The place chosen for the observations was the physiology department, since adequate measuring apparatus and a quiet room in which outside influences could be partially controlled were available there. Conditions for the observations were maintained as nearly standard as possible. Since it was impossible to control the patient's mood or to put her in a particular one at will, an analysis of her mood was made without her knowledge at the time of each observation. This was done constantly by the same observer, and it was soon clear that her moods fell into several categories which seemed readily classifiable. All possible moods were obviously not represented, and no active attempt has been made to create situations for their effect since it was felt that the artificial factors involved might undermine the confidence of the patient. On the whole, we believed that the external factors were well controlled and that, within limits, comparable observations were carried out.

Recordings were obtained of the motility of the antral region of the stomach by means of a rubber balloon attached to glass tubing which recorded on a smoked drum by means of a tambour connected to a manometer containing solution of sodium chloride. An attempt was made to insert the balloon to the same point and with the same pressure each time. The secretion of the stomach was allowed to flow out of the fistula by gravity and was collected in a glass beaker. The gastric juice was analyzed for combined and free hydrochloric acid, pepsin and bile; the general character of the secretion was noted, and subjective sensations, such as hunger pangs and heartburn, which occurred during observation were

recorded. The color of the mucosa was observed by means of a constant light source and compared directly with a Tallqvist hemoglobin scale. All the observations began at 8:00 to 8:30 a.m., and for each the patient had been fasting for approximately twelve hours unless otherwise indicated.

Findings.—Several control observations were made in the hope of determining the behavior of the stomach in standard circumstances. As indicated previously, these were done under constant environmental conditions, and the patient's mood was recorded at the time of each observation. On this basis, seven observations over periods ranging from one to three hours each were made during which the patient appeared cheerful, happy and cooperative. In the following presentation these normal or control studies will be compared with three studies made during periods of emotional tension. To clarify the description of our findings, several subheadings will be used.

Motility: In five of the seven control observations the motility followed a characteristic pattern. Cyclic activity occurred, with the cycles ranging from fif-

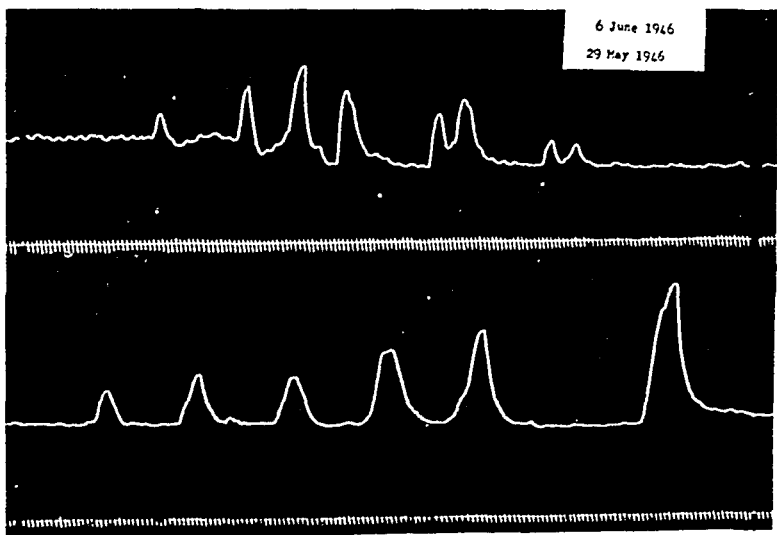


Fig. 2.—Photographs of kymographic recordings of normal peristalsis in the antrum of the stomach on two occasions which illustrate common types of contractions. Time is recorded at second intervals, and a complete cycle is shown in each recording. Note in the lower recording a gradual increase in the amplitude of the peristaltic wave, with no increase in the tone of the stomach as indicated by the base level of recording.

teen to forty-five minutes apart. Occasionally isolated contractions would occur. Two types of contractile activity were observed by us. The higher, rhythmic waves of contraction advancing toward the antrum were noted to be peristaltic in type and seemed to have a propulsive effect on the balloon (fig. 2) The other type was an irregular contraction of lesser magnitude, and it can best be described as a massage or mixing type of activity. We did not note changes in the tone of the stomach with increasing amplitude of contractions. This is clearly illustrated in the lower recording in figure 2. There is no gradual increase to a state of tonic contraction such as has been observed in the male by Wolf and Wolff.⁴ Most of the contractions seen at the time of the control observations were of the peristaltic type, and during activity they would occur at the rate of two to three per minute. The average recorded duration of the contractions was usually fif-

teen seconds. In two of the seven observations no motility at all was recorded during a period of three hours. No reason for this lack of motility was apparent. In the determination of the degree of motility of the stomach, the average number of contractions per unit of time was used, with the entire period of the observation entering into the calculation. On this basis, it was found that contractions occurred at the average rate of one every 3.4 minutes during the four periods of observation in which the typical peristalsis was observed (fig. 3). However, several incidental factors were noted which were of interest. Any distention of the recording balloon led to an immediate local contraction of the stomach. This usually subsided quickly and did not influence or initiate any cyclic type of activity. This is in agreement with a similar observation made by Carlson on Mr. V.³ However, Wolf and Wolff failed to obtain a similar result.⁴ Distention, they found, was followed either by relaxation or by a change in the level of the base line of recording.

When appetizing food was shown to Doris, it was found to cause a contraction of the stomach wall, which subsided quickly and did not continue. During one observation, she reported hunger pangs at a time when no contractions were recorded. At another time she complained of cramping pain during exceptionally strong contractions of the stomach, followed by a feeling of hunger. We, as well as Wolf and Wolff, therefore are unable to confirm Carlson's observation that the sensation of hunger is always accompanied with contraction of the stomach.

Secretion: The character of the gastric secretion was rather constant. Usually it was mucoid in character, and in some instances it was slightly bile-tinged. It also appeared that with increased motility the rate of secretion increased. This may have been the result of better emptying of the stomach with increased tone, but this seems unlikely inasmuch as free flow occurred at all times. At any rate, the amounts were purely relative since the entire gastric secretion was never obtained. It was interesting to note that the amount of secretion seemed to have a direct relation to the color gradient of the gastric mucosa. As has been noted, the color gradient was obtained by direct comparison of the gastric mucosa with a Tallqvist hemoglobin scale. The amount of secretion increased with an increase in the color gradient. For example, on one occasion on which there was an average color gradient of 70 the secretion collected during a period of seventy-five minutes was 64.4 cc., with 60 degrees of free hydrochloric acid and 18 degrees of combined acid, or a total of 78 degrees of hydrochloric acid. Study of motility showed an average of one contraction in two minutes. This observation was made the third day of menstruation. On a second occasion, when the color gradient averaged 55 the secretion was 55 cc. in ninety-five minutes or 43.5 cc. in seventy-five minutes. Some of this secretion contained bile, with no hydrochloric acid and 10 to 15 degrees of combined hydrochloric acid. There was one contraction every two and a half minutes. On a third occasion, when there was an average color gradient of 45 to 50 the collected secretion over a period of one hundred and ten minutes was 16 cc., with no free hydrochloric acid and 15 degrees of combined acid. No motility was noted during this observation. All these observations were made while the patient was considered to be in a cheerful and cooperative mood. The average color gradient was 50 to 55, with a maximum of 75 and a minimum of 40. The lower color gradient, when it appeared, was present for only short periods. Periods of sleep during the observations appeared to have little or no effect on the color, secretion or motility.

In contrast, three observations were made at times when Doris was disgusted, sullen and angry. This mood was due to what appeared to her as procrastination

and neglect in her treatment. When she was seen in this mood, no attempt was made to change it until after an observation had been made. The accompanying table records seven typical observations indicating the reactions of the stomach to various moods. In experiment 1 the increased acid is probably due to a recent feeding which had to be evacuated from the stomach. The increased motility in experiment 2 as compared to 1 and 3 is probably due to discomfort. The contractions occurred during the first fifteen minutes of the observation, with no contractions during the remainder of the observation. The most constant changes noted are increased motility and increased color gradient when the mood was one of happiness. It is better to examine these three observations separately.

When the observation was made on Feb. 4, 1946, Doris was found to be disgusted with the whole situation, as well as being obviously disappointed. She had been fed two and a half hours before on this occasion, but her stomach was emptied for a control period. The motility of her stomach was found to be

Reaction of the Stomach to Various Moods

| Experiment | Condition of Stomach | Mood | Motility (Contractions Per Hr.) | Secretion (Cc. per 5 Min.) | Acid† | | Color |
|------------|----------------------|---------------------|---------------------------------|----------------------------|-------|----------|-------|
| | | | | | Free | Combined | |
| 1 | Not fasting* | Angry and resentful | 5 | 1.1 | 50 | 20 | 45 |
| 2 | Fasting 12 hours | Angry and resentful | 20 | 2.5 | 0 | 39 | 35 |
| 3 | Fasting 12 hours | Angry and resentful | 6 | 0.8 | 0 | 10 | 45 |
| 4 | Fasting 12 hours | Happy | 10 | 2.7 | 0 | 39 | 50 |
| 5 | Fasting 12 hours | Happy | 19 | 3.3 | 60 | 18 | 65 |
| 6 | Fasting 12 hours | Happy | 23 | 1.4 | 30 | 10 | 50 |
| 7 | Fasting 12 hours | Happy | 25 | 3.0 | 0 | 15 | 55 |

*Liquid feeding given one hour before was evacuated from the stomach prior to observation.

†Measured in degrees of hydrochloric acid, 1 degree being the amount neutralized by 0.1 cc. of tenth-normal sodium hydroxide.

markedly depressed, peristalsis occurring only when she was shown some appetizing food. This peristalsis quickly subsided, however. The secretion which had measured only 26 cc. in the previous hour, increased to 20 cc. in the first ten minutes after appetizing food was tasted. The secretion before and after the patient saw appetizing food contained 50 degrees of free acid and 20 degrees of combined acid even though none of the food reached the stomach at any time. The color gradient of the mucosa was not accurately followed every five minutes during this particular observation, but it was noted that after being told of a proposed operation the patient showed a response of moderate fear and the color gradient of the gastric mucosa decreased from 50 to 40 (experiment 1).

A somewhat different picture was seen on Feb. 6, 1946, at which time Doris was sullen and defiant and on the point of refusing to submit to the observation. Her answers were short, and she was extremely uncommunicative. She did what she was asked to do but obviously under protest (experiment 2).

At this time the motility was cyclic in type, with large peristaltic contractions occurring in three cycles during a period of seventy minutes. During the periods of activity, the contractions occurred every thirty seconds, with a total of twenty-four contractions, or approximately an average of one every three minutes. Doris complained of cramping pains with some of the stomach contractions and a pronounced feeling of hunger which was present after the contractions stopped. The color gradient was exceedingly low during this observation, i.e., 30 to 35, as was the secretion, except during the period when the hunger contractions were occurring, at which time the color gradient increased to 45 and the amount of secretion increased markedly. After the subsidence of motility, the color gradient fell again to 30 and the secretion became meager in amount. The secretion was thick in character and was grossly bile tinged. No free acid and 30 degrees of combined acid were found in the specimen of secretion.

On May 3, 1946, the patient was again found to be upset and disgusted because of what she considered procrastination in her care. This observation was made on the third day of her regular menstrual period. In spite of her mental

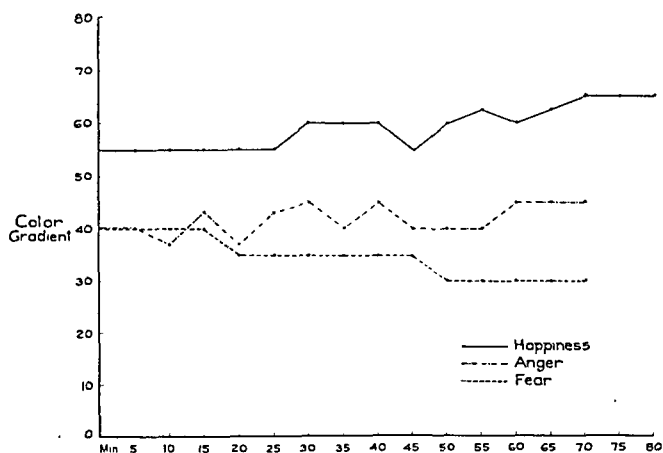


Fig. 3.—A composite graph of the observations of the color of the gastric mucosa (i.e., color gradient) made during periods when the patient was happy, angry and fearful. Note that happiness is associated with a greater color gradient than anger or fear. This is in contrast to the usual observations made on male patients.

state, she was cooperative. During the early part of the observation, the stomach was found to be active for a period of approximately fifteen minutes. The contractions were of the message type rather than peristaltic, being low in amplitude and of much higher frequency. The rate was five to seven per minute. These probably were secondary to the pain associated with insertion of the recording balloon. After cessation of this activity, no further activity occurred for a period of one hour. The secretion was small in amount, measuring 25 cc. in one hour and forty-five minutes. The color gradient ranged between 40 and 45, with little variation. The secretion was mucoïd and yellow. No free acid and 10 degrees of combined acid were found (experiment 3).

These observed effects are interesting in view of their variance from those noted by Wolf and Wolff. They found that anger, resentment, hostility, anxiety and sustained emotional tension led to hyperemia, hypersecretion and hypermotility of the stomach. Fear and depressing thoughts led to depressed secretion and motility and to blanching of the mucosa. Our patient showed depressed se-

cretion and motility and blanching of the mucosa not only when she was fearful but at each time when she was considered to be angry, resentful and anxious as to the outcome of her treatment.

Effect of Menstruation: Two observations during the control period were made on the third day of the patient's menstrual periods (Feb. 25 and May 3, 1946). On February 25, however, she was cooperative and happy, while on May 3 she was disgusted and disappointed. Apparently the only common factor was a short period of increased motility, although it varied somewhat in type. As to secretion, hydrochloric acid and color gradient, opposite ends of the scale were reached; they followed the mood rather than the menstrual phase. From the small number of observations made, little correlation with the menstrual period can be made.

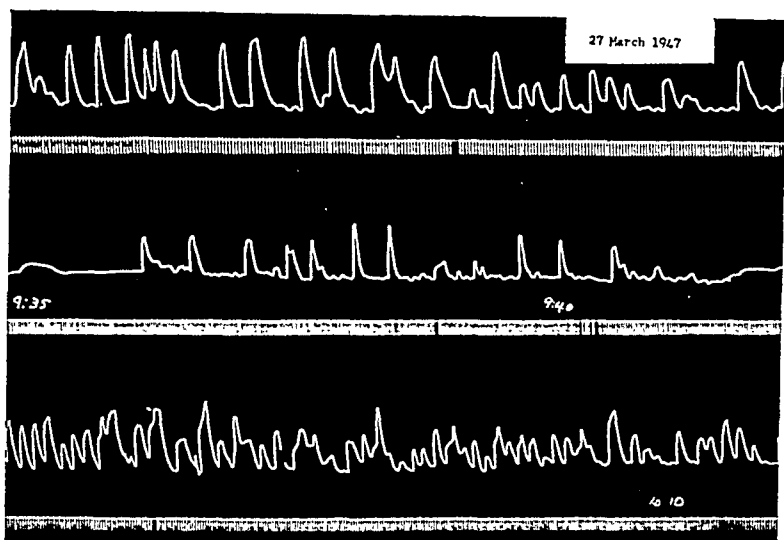


Fig. 4.—A photograph of actual kymographic recordings, showing the response to a painful stimulus. Time is recorded in seconds. The upper recording was made during the period immediately following the insertion of the latex balloon into the pyloric antrum, which caused moderate pain. The increased and rather irregular motility can be compared to that demonstrated by the middle recording, which shows a cycle of motility recorded fifteen minutes later while the patient was free of pain. The lower recording was made later during the same observation at a time when there was pain induced by a rather difficult venipuncture. As can be noted, pain caused a decided increase in motility of the stomach.

On several occasions attempts were made to pass catheters through the cardiac sphincter of the stomach into the esophagus by means of a specially constructed instrument similar to an extremely large sigmoidoscope. This was successful on 2 occasions. During these procedures several observations were made which may be of interest. The cardia was radially scarred but showed a definite rhythmic type of motility. Slow waves of contraction and relaxation occurred, but it was impossible to determine through our instrument whether they were propagated onto the stomach wall. The rate was similar to that observed in the stomach, however, and there were periods when no motility was observed in the cardiac sphincter.

When a catheter was placed in the cardiac sphincter and slight pressure applied, severe retching and heartburn occurred. A considerable increase in bile-

stained secretion also occurred, presumably due to regurgitation through the pylorus. It would stop immediately with removal of the catheter. The stimulus apparently was mechanical, since the onset and the end of the symptoms occurred immediately with pressure changes, although the catheter could be left in contact with the mucosa. A smaller gage catheter could be passed without producing nausea or retching and causing only transient heartburn.

The pylorus was also observed on several occasions, but it was found to be closed at the time of each observation.

During the course of subsequent observations, it was noted that painful stimuli, such as venipuncture, muscle cramps or the insertion of the recording balloon, which usually caused mild discomfort, were nearly always followed by a striking increase in the motility of the stomach. Secretion and color gradient were apparently not altered. Relief of the pain usually resulted in the return of the stomach to a state of activity comparable with the state existing before the painful stimulus was experienced (fig. 4).

SUMMARY

Direct observations of the interior of the stomach were made through a large gastrostomy opening in a 21 year old Negro woman.

A cyclic motility was observed. The interval between cycles and the magnitude of contractions varied considerably. Two types of contraction were seen, i.e., a basic kneading type and a peristaltic type. A cyclic type of motility at the cardiac sphincter was noted.

Under standard conditions, with the patient fasting and in a happy and cooperative mood, a moderately active, secreting stomach with a relatively red mucosa was observed.

Anger, resentment, fear and anxiety were associated with decreased motility and secretion of the stomach and with blanching of the mucosa. It was also noted that the secretion had a lower hydrochloric acid content.

Heartburn, nausea, retching and a reflex of bile-stained secretion were caused by mechanical stimulation in the region of the cardiac sphincter.

Menstruation did not have any appreciable effect on the observed behavior of the stomach.

Periods of sleep appeared to have little effect.

Painful stimuli caused a pronounced increase in the motility of the stomach but had little effect on the secretion or on the color gradient.

The absence of hypersecretion and hypermotility under conditions of sustained emotional tension in this patient was in striking contrast to their presence in male patients previously studied.

EFFECT OF INTRAVENOUSLY ADMINISTERED AMINO ACIDS ON THE STOMACH OF A WOMAN WITH A GASTRIC FISTULA

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THE PURPOSE of this study was to observe directly the effects on the stomach of giving various fluids intravenously, especially those used frequently for intravenous feeding. These observations were made on the interior of the stomach of a 21 year old Negro woman, D. B., through a large gastrostomy opening 6 cm. in diameter.

METHOD OF PROCEDURE

The motility of the stomach was recorded by means of a rubber balloon (condom) which was connected through a glass tubing with a manometer filled with solution of sodium chloride which in turn was connected to a tambour for kymographic recording. Gastric juice was allowed to flow by gravity into a glass beaker by having the patient lie on her left side. Values for hydrochloric acid were obtained by titration with tenth-normal sodium hydroxide, Toepfer's reagent and phenolphthalein being used as indicators. Pepsin values were obtained by the Metz method. The blood flow was expressed as a color quotient, which was expressed in terms of hemoglobin concentration by direct comparison of the gastric mucosa with a Tallqvist scale. For all observations standard conditions were maintained; the patient had been fasting for twelve hours and was cooperative and happy except on occasions indicated.

After control periods of observation, various fluids were given intravenously. These included (1) a solution containing 5 per cent hydrolyzed protein ("amigen") with 5 per cent dextrose and 2 Gm. of sodium chloride per liter (given on two occasions), (2) a solution of crystalline amino acids (Merck & Co.) in 5 per cent dextrose, (3) a solution of 10 per cent dextrose in water, (4) a solution of 10 per cent dextrose in water, containing 2 Gm. of sodium chloride in 1,000 cc. and (5) isotonic solution of sodium chloride. The patient was somewhat fearful of the venipuncture because of previous experiences, but her reaction was relatively constant for all the fluids given, and the effect was thought to be essentially the same in each instance. No attempt was made to hide what was going to be done except that no indication was given of which fluid was being injected.

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FINDINGS

1. Two observations were made during the intravenous injection of 1 liter of fluid containing 5 per cent hydrolyzed protein ("amigen") and 5 per cent dextrose with 2 Gm. of sodium chloride. On May 20, 1946, the patient was as usual apprehensive at the prospect of a venipuncture, but she was cooperative. She had been fasting for twelve hours. There was a fifty minute control period before the administration of "amigen" was started, and during it the stomach was active, undergoing contractions of the peristaltic type that were cyclic in character, occurred at a rate of two per minute and lasted fifteen to twenty seconds. There was a total of forty-five contractions in fifty-five minutes. The color gradient was 45 to 50, and the secretion was 20 cc. in forty minutes; the latter contained no free hydrochloric acid and 24 degrees of combined hydrochloric acid.

Immediately after the start of the injection of "amigen" the motility continued, but the earlier slow, rhythmic, propulsive type was replaced by nonpropulsive, massage-like contractions. This effect was probably due to the pain of the venipuncture, as it was similar to that observed at other times after painful stimuli, i.e., the curves showed a more irregular but more rapid rate of contractions of lower amplitude. The type of contractions described gradually decreased in amplitude until they disappeared completely thirteen minutes after the administration of "amigen" was started; they did not recur until approximately two minutes after administration was discontinued fifty minutes later. This recurrence was assumed to be due to the pain of removing the needle.

The rate of flow at the start was 15 cc. per minute, which is more rapid than usual. The faster rate was chosen to observe the effect of nausea, which frequently follows after such a rapid rate of administration. As was expected, the patient complained of feeling slightly nauseated when approximately 200 cc. had run in. The stomach in the meantime had become quiescent, and the secretion had fallen off sharply, was almost entirely mucoid in character and contained bile. The patient became quiet as though she were asleep. She then complained of thirst; the color gradient was measured and found to be 30. During all this time, the secretion was extremely meager. At no time during periods in which she complained of nausea was there any motility of the stomach even though there was considerable salivation.¹ No free acid and 36 degrees of total hydrochloric acid were found in the gastric secretion.

A second injection was given on June 7, 1946, which was on the second day of the patient's regular menstrual period. Although fearful

1. Wolf, S.: The Relation of Gastric Function to Nausea in Man, *J. Clin. Investigation* 22:877-882, 1943.

of the pain produced by the needle, she was cooperative and cheerful. During a thirty minute control period the stomach was exceedingly active and showed the usual contractions. The color gradient was 40 at the onset and gradually fell to 30. No free acid and 26 degrees of combined hydrochloric acid were found in the gastric secretion during the control period.

After the needle was first introduced, the stomach showed the same changes as those described previously, which were interpreted as being due to the pain stimulus. After this period of activity, there was complete quiescence except during one or two short intervals in which the amount of secretion gradually dropped to zero, with the color gradient remaining at 30. There was also no change in the hydrochloric acid content. Determinations of pepsin content made at the same time showed a drop to one third of the fasting level. This finding may be questioned, however, since the pepsin content of the specimen obtained when the stomach was first emptied was twenty times as high as that in the specimen obtained after "amigen" was given. Practically no nausea was observed during this injection, which was due to the slower rate of injection (10 cc. per minute). In summary, at the time of both observations there was a cessation of preexisting motility and a decrease in secretion, without any appreciable change in the acid content but with a decrease in the pepsin content.

2. One observation was made on May 29, 1946, on the use of 10 per cent dextrose in water. The patient's mental state was little changed from that found at the time of the other observations. She apparently had been angry with one of the nurses before coming to the laboratory, but she was in good spirits at the time. A control period of approximately thirty minutes was observed. The patient had taken a small amount of food five hours before, but this was removed completely before the observation was begun. During the control period, typical cyclic peristalsis was seen. The secretion was small in amount and rather thick and mucoid in character. It was bile tinged and contained no free acid and 58 degrees of combined hydrochloric acid. The color quotient was found to be 40 to 45.

After the injection was started no change could be seen in the motility with the exception of a slight increase in the rate of contractions. There was little change in the amount of secretion, two specimens containing 30 and 55 degrees of combined acid respectively. The pepsin content, however, was observed to drop to one third of the fasting value. No change in the color quotient was noted. The patient's only complaint during the observation was of a full feeling in her stomach and a transient chilly sensation. The rate of flow was controlled as nearly as possible at 15 cc. per minute. In summary, no change was observed during the injection of 10 per cent dextrose in water.

DIAGNOSIS

The symptoms of duodenal ileus are often misinterpreted, so that a correct diagnosis is not made until the duodenum is exposed during an exploratory operation. Even the roentgen ray may not clearly define the condition.

When patients with visceroptosis complain of the symptoms listed above the presence of duodenal ileus should be suspected. The vomiting of large amounts of bile stained fluid with evidence of retention, especially if associated with severe headaches, should arouse suspicion if other pathologic conditions can be ruled out. Barker lays stress on the examination of the vomitus for the presence of bile and pancreatic juices, as he states that the ducts empty into the duodenum and the presence of the juices in the vomitus would be evidence of regurgitation from the duodenum. As we know, the duct of Santorini opens above and in front of the common duct and the main pancreatic duct. Thus, if an obstruction lies between these two ducts there would be pancreatic ferments but no bile in the vomitus. The presence of pancreatic ferments is tested by fibrin digestion. The acid present in the fluid is neutralized and the fluid is then rendered slightly alkaline. A flake of fibrin stained with magenta red is then placed in the solution and incubated. If the fibrin is digested the fluid becomes red.

Hayes⁵¹ suggests that the presence of tympany in an area behind the right rectus muscle and to the right or posterior to the pylorus between the transverse colon and liver indicates dilatation of the duodenum.

Zade⁵² emphasized the value of the stomach tube for diagnosis as it makes it possible to differentiate between an hour glass stomach and a dilated duodenum in cases in which the symptoms suggest either of these conditions. His method is to compare the amount of water passed into the stomach through a stomach tube with the amount siphoned off, this procedure being followed by studying the tympanitic area on the abdomen. He found that in cases with pyloric relaxation and a dilated duodenum the pouch, which became filled with the residual water after the stomach was emptied, was well to the right of the midline.

The history and physical findings are important as has been shown by the fact that in a few of our cases a correct diagnosis was made before the roentgen-ray examination, but roentgen-ray and fluoroscopic examinations are of considerable value in many cases. Sometimes evidences of antiperistalsis with regurgitation of the barium meal into the stomach or of duodenal stasis may be secured by the fluoroscope, while

51. Hayes, W. V.: A Few Signs Helpful in the Diagnosis and Management of Chronic Intestinal Stasis with Some Suggestions as to Treatment, *Internat. J. Surg.* 27:134-136, 1914.

only a questionable roentgenogram is obtained. It should be realized that a pathologic condition may be present in the duodenum even if the duodenal cap fills perfectly. To eliminate duodenal stasis the duodenum should be observed at intervals for a period of from twenty to forty-five minutes. In many instances enteroptosis or gastropstosis render visualization of the third portion of the duodenum difficult and a lateral view must be taken to secure a good picture.

Obstruction of the second portion is more readily visualized as the dilatation is frequently above the transverse colon and is seen at the right of the stomach.

Delay in the passage of barium through the duodenum (duodenal stasis) is suggestive especially if the duodenum is constantly visible. Hayes' technic for visualization of the duodenum should be used in suspected cases.

Of course in all cases of acute dilatation of the stomach the condition should be suspected and an attempt should be made to see whether change of posture will relieve the symptoms.

TREATMENT

Many cases of arteriomesenteric ileus progress satisfactorily with nonoperative therapy. As has already been suggested, the knee-chest position may give relief; lying on the abdomen also relieves the mesenteric pull. Lying on the right side with the hips elevated tends to facilitate duodenal elimination and diminishes traction on the mesentery across the duodenum.

The knee-chest position should be assumed for fifteen minutes out of every two hours. Mechanically this relieves compression on the duodenum as the interior abdominal wall tends to bear the weight of the viscera. Duodenal lavage with the duodenal tube is of value. Carbohydrates should be prescribed and in general the diet should be of high caloric value and low in ferments. A corset should be applied (with the patient in the heel-shoulder position in cases of enteroptosis). Exercises for the strengthening of the abdominal wall should be insisted on.

If adequate medical treatment fails to alleviate the discomfort a duodenojejunosomy should be performed.

DUODENOJEJUNOSTOMY (CRILE TECHNIC)

In a duodenojejunosomy (Crile technic) the transverse mesocolon is exposed and the duodenum is exposed by an opening over its third part.

The anterior wall of the duodenum is picked up with Ally's clamps (care being taken that it is entirely free). The jejunum also is picked up with Ally's clamps, from approximately 7 to 10 cm. from the fossa



does not pass through the dilated pylorus and that therefore some stasis will be present in the dilated duodenum.

Other surgeons recommend resection of the right colon combined with an ileostomy which may be performed with safety in one stage. The end-results in these cases are also satisfactory.

In reviewing the opinion of various physicians and surgeons we find that duodenojejunostomy is favored by Barker, Bloodgood, Crile, Jones, Lower, Stavely, Tinkham, Vanderhoof and Wilkie, and that most surgeons agree that duodenojejunostomy is the method of choice if the obstruction is due to the mesentery. If the obstruction is due to adhesions they should be separated by sharp dissection, and if the duodenum is atonic a duodenojejunostomy also should be performed. If coloptosis is present resection may be deemed advisable. Robinson has reported three cures after gastro-enterostomy.

Results

| Treatment | Number of Cases | No Improvement | Improved | Improved but Too Early for Conclusions | Complete Relief | No Report |
|-------------------------|-----------------|----------------|----------|--|-----------------|-----------|
| Medical..... | 31 | 2 | 19 | 2 | 1 | 7 |
| Medical and surgical... | 3 | .. | 1 | .. | 2 | .. |
| Surgical..... | 20 | .. | 7 | 1 | 12 | .. |

Three additional cases have been diagnosed; two of the patients are to return for operation; medical treatment was recommended for the third.

COMPLICATIONS

Wilkie states that ulcers may be associated with dilatation of the duodenum and reports three cases. I am reporting five such cases.

Kellogg and others believe that the stasis predisposes to ulceration. Codman cites Türck's studies of the effects of feeding food saturated with *Bacillus coli* to dogs. In twelve cases ulcers of the stomach and duodenum developed. He raises the question as to whether bacterial growth favored by stasis might not act similarly.

Cholecystitis or pancreatitis due to ascending infection along the ducts may occur.

MORTALITY

In our series there have been no deaths that could be directly attributed to surgical intervention. In one case in which miliary tuberculosis was found at operation, the patient died later from Addison's disease. In another case death was due to carcinoma of the sigmoid. The cases in which persistent vomiting necessitated surgical procedures progressed favorably.

In every case in which duodenojejunostomy was performed, except that of the patient who died of Addison's disease, complete relief was

obtained. In one case in which gastro-enterostomy was performed, periodical attacks of vomiting have continued so that a duodenojejunostomy will be performed later.

Thirty-four patients have been treated medically. In three cases among these the persistent vomiting necessitated an operation. Two patients were improved to such an extent that operation was not deemed necessary; in one case the symptoms were completely relieved. Seven patients have failed to answer the letter of inquiry regarding their present condition, and a few patients have improved, but sufficient time has not elapsed to warrant definite conclusions regarding their status.

CONCLUSIONS

Chronic duodenal ileus is not a rare condition and there are undoubtedly many cases that have not been diagnosed. On account of the severe headache associated with this condition a diagnosis of migraine is usually made; some patients have been treated for migraine for years and have passed through the clinics of excellent diagnosticians in a search for relief. In all cases of severe headache associated with vomiting a careful examination of the duodenum should always be made.

In cases in which the dilatation is insufficient to produce duodenal stasis and is associated with gastropnoia, an effort should be made to secure relief by nonoperative measures. If the dilatation is marked and stasis with antiperistalsis is present, a duodenojejunostomy should be performed. The mortality for duodenojejunostomy is practically nil and excellent results may be expected. Resection of the right colon is indicated in few cases and should be performed only as a last resort. Gastro-enterostomy should not be performed, as the stasis in the duodenum is not relieved and a vicious circle is established. A careful roentgen-ray examination of the duodenum should be made and a correct preoperative diagnosis established. A comprehensive history and a careful physical examination may suffice to make a correct diagnosis which, however, should be verified by roentgen ray. Dilatation of the duodenum is a clinical entity and a characteristic picture is present in most of the cases.

REPORT OF CASES

PATIENTS RECEIVING MEDICAL TREATMENT ONLY

CASE 1.—A woman, aged 24, came to the clinic because of pain in the stomach. For the preceding two years she had suffered from pain in the abdomen, which often occurred from three to four hours after meals. On account of the formation of gas she was unable to eat meats, acids or carbohydrates. The bowels were costive. At times during the night she would waken with a sensation of heaviness in the stomach.

The only important facts elicited by examination were the evidences of gastropnoia, anemia, and tenderness on deep pressure over the stomach below

the ensiform. Roentgen-ray examination showed marked stasis, with delay in the duodenum and reverse peristalsis. The stomach and duodenal cap filled normally.

The laboratory findings were: urine, normal; hemoglobin, 85 per cent.; red blood cells, 4,120,000; white blood cells, 6,400.

A diagnosis of dilatation of the duodenum was made. Medical treatment, consisting of a special corset, exercises, rest and diet, was instituted. Two months later the patient was having attacks of vomiting but she did not return for further treatment.

CASE 2.—A boy, aged 7 years, entered the hospital because of pain in the upper epigastrium. A history of pertussis and chickenpox was given. For the last few months the child had complained of pain in the epigastrium, occasionally quite severe. The temperature at times was from 99.2 to 99.4. The bowels were costive. Vomiting occurred during the acute attacks. For the preceding eight months he had been on a diet from which sugar, milk and fats were practically eliminated.

The only significant points disclosed by the physical examination were that the boy was poorly nourished, pale and underdeveloped, with an abdomen of the visceroptotic type.

The laboratory findings were: urine, normal; hemoglobin, 70 per cent.; red blood cells, 4,130,000; white blood cells, 6,600.

The roentgen-ray examination revealed an incomplete obstruction at approximately the point where the superior mesenteric artery and mesentery crossed the spine. Above this point the duodenum was dilated and reverse peristalsis was present. A diagnosis of dilated duodenum was made.

The application of a binder and special diet were advised and improvement resulted.

CASE 3.—A woman, aged 56, entered the hospital because of attacks of stomach trouble. For twelve years the trouble had been more or less constant, the attacks increasing in severity and frequency. During the preceding five months she had lost 30 pounds (13.6 kg.). The attacks consisted of dull, non-radiating aching in the epigastrium. This came on a few minutes after meals and persisted until she vomited. Severe headaches accompanied the attacks. For a long time she had not eaten an evening meal so that she would avoid vomiting at night. Solid food aggravated the condition, fluids causing less discomfort. More recently she had had a sour stomach and heartburn. She had been on liquid diet for the preceding two weeks.

Examination disclosed an anemic, poorly nourished woman, with evidences of loss in weight. Tenderness was present over the entire abdomen, which was relaxed.

The laboratory findings were: urine, normal; hemoglobin, 70 per cent.; red blood cells, 3,990,000; white blood cells, 5,000; Wassermann reaction, negative. Gastric analysis revealed: free hydrochloric acid, 65; total, 79; lactic acid and bile were absent.

The roentgen-ray examination disclosed a dilated duodenum which retained barium after the stomach was empty.

Under medical treatment consisting of rest after meals, hyperacidity diet and postural exercises, some improvement resulted, but not complete relief of symptoms.

CASE 4.—A man, aged 36, entered the clinic complaining of stomach trouble. There was no point of interest in his personal history except a previous attack of influenza.

For the last three weeks he had had more or less constant abdominal discomfort. He stated that all the food he ate seemed to sour and to cause pain in the epigastrium; this was relieved by vomiting. The pain usually occurred from one to three hours after meals. The bowels were regular. There was tenderness to palpation in the epigastrium.

The laboratory findings were: urine, normal; Wassermann reaction, negative; hemoglobin, 80 per cent.; red blood cells, 4,780,000; white blood cells, 11,000; differential blood count, normal. Gastric analysis revealed: total acidity, 98; free acid, 64; bile, 3 plus.

The roentgen-ray examination showed that the first part of the duodenum was markedly dilated, and that it did not empty unless pressure was applied from above.

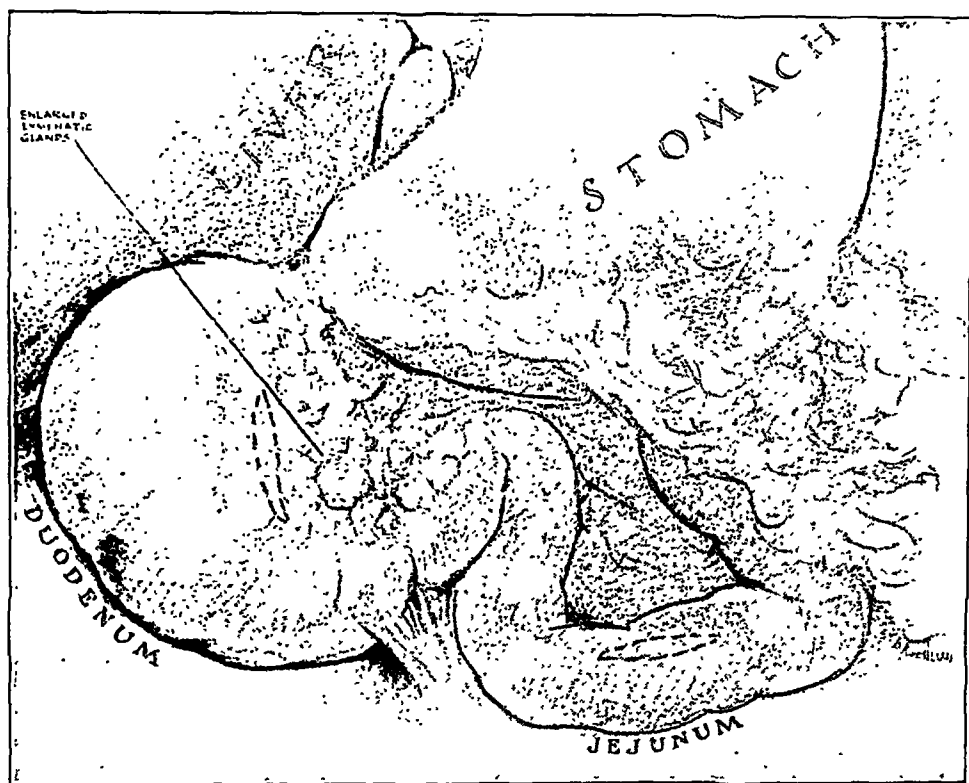


Fig. 3.—Duodenojejunostomy for megaduodenum in little girl, aged 5 years; broken lines represent points of approximation for the anastomosis.

Medical treatment, consisting of diet and postural exercises, was begun. Some improvement resulted, but the patient failed to report for later observation.

CASE 5.—A man, aged 32, entered the clinic complaining of pain around the heart. He gave a history of a previous attack of typhoid. For the last two weeks he had experienced pain that came on suddenly when he stooped over to remove his shoes. Pain also occurred before and after meals. He was short of breath on exertion. His bowels were costive; his appetite was good; he was gaining in weight. Fulness in the upper part of the abdomen was present at irregular intervals.

Physical examination revealed a blood pressure of 100 systolic, 70 diastolic; slight exophthalmos with no enlargement or increased activity over the thyroid; a considerably relaxed abdominal wall. The heart and lungs were normal.

She was occasionally nauseated and sometimes vomited. She dated the onset of the headaches from an attack of cerebral meningitis fifteen years before, at which time she was confined to her bed with fever, stiff neck and attacks of unconsciousness. The pain had become more severe during the last few years, and was worse during the menses.

A diagnosis of migraine and of neuralgia of the great occipital nerves had previously been made, and an injection of the sphenopalatine ganglion had been performed.

The physical examination failed to elicit any important points. The gastric analysis revealed: total acid, 85; free acid, 32.5. Other laboratory findings were normal.

A roentgenogram was taken which showed a mobile, dilated pelvic cecum, and dilatation of the second and third portions of the duodenum.

A diagnosis of dilatation of the duodenum was made and medical treatment—corset, diet, postural exercises, diluted hydrochlorid acid and iron—was instituted. The condition of the patient improved, but too short a period of time has elapsed to warrant definite conclusions.

CASE 9.—A woman, aged 32, entered the clinic complaining of stomach trouble. A thyroidectomy had been performed in 1908, a nephrectomy in 1916, an appendectomy in 1921. For several years the patient had had a dull, aching pain in the upper part of the abdomen which was not associated with vomiting, though she had some nausea. She had frequent headaches which were accompanied by gastric disturbances. The bowels were costive. After the thyroidectomy the patient had developed tetany, which has persisted in spite of treatment.

Physical examination elicited tenderness and spasm on pressure over McBurney's point.

The laboratory findings were: blood and urine, normal; Wassermann reaction, negative.

The roentgen ray showed the second and third portions of the duodenum to be considerably dilated.

A diagnosis of dilatation of the duodenum was made and medical treatment was instituted, as the result of which the patient reports that most of her abdominal discomfort has been relieved.

CASE 10.—A man, aged 62, entered the clinic complaining of headaches and bilious attacks. His father had died of an aneurysm. The onset of the bilious attacks dated back ten years, and the headaches had occurred even previous to that time. The attacks began with severe headaches and sour stomach, which were relieved by soda or copious emesis; diarrhea occurred during the attacks. The bowels were fairly regular. He formerly belched considerably.

Physical examination revealed an asthenic type of man. The left colon was palpable, and the stomach was palpable below the umbilicus.

The laboratory findings were: urine, normal; Wassermann reaction, negative; hemoglobin, 85 per cent.; red blood cells, 3,980,000; white blood cells, 5,300.

The roentgen ray showed a dilated duodenal bulb and an elongated and moderately enlarged duodenum, with stasis; ptosis of the cecum also was present.

A diagnosis of dilatation of the duodenum was made and medical treatment was instituted. The period of time that has elapsed since treatment was started is insufficient to warrant definite conclusions.

CASE 11.—A woman, aged 21, entered the clinic complaining of a goiter and of stomach trouble. She had previously been operated on for appendiceal abscess and had had a dilatation and curettage. The illness of which she

complained at this time had begun a year before with nervousness, palpitation, loss of weight and tremor. She was subject to epigastric pain and right-sided headache which usually came on about noon. These symptoms were relieved by vomiting. The vomitus was yellowish brown and often contained food particles.

Examination showed that she had a bilateral enlargement of the thyroid, with a small adenoma on the right; also tenderness with spasm in the outer upper quadrants of the abdomen, most marked on the left.

Laboratory examination showed the blood and urine to be normal.

Roentgen-ray examination disclosed a duodenal dilatation with stasis, and a mobile, slightly ptosed cecum. A diagnosis of dilatation of the duodenum was made, and medical treatment was instituted with resultant improvement.

CASE 12.—A man, aged 45, entered the clinic complaining of stomach and bladder trouble. He had had an appendectomy twenty-two years before, and a cystostomy seventeen years before. He had had "bloating" of the stomach for years, the discomfort arising immediately after each meal and lasting for approximately one hour. At this time he had nocturia once each night. He was quite constipated, was nervous and at any new shock experienced a "gripping" of the stomach. His weight was stationary.

Physical examination revealed evidence of gastroptosis and spasticity of the transverse and descending colon.

The laboratory findings were: urine, normal; Wassermann reaction, negative; hemoglobin, 80 per cent.; red blood cells, 4,120,000; white blood cells, 5,800; differential count, normal.

Roentgen-ray examination showed the stomach to be normal; marked hypermobility of the duodenal bulb, which was dilated; dilatation of the second and third parts of the duodenum, and a small stone in the lower part of the left ureter.

A diagnosis of dilatation of the duodenum and of left ureteral calculi was made, and medical treatment was instituted. No report has been received from this patient.

CASE 13.—A woman, aged 48, entered the clinic because of headaches. For some time she had had headaches which were periodic in type, and usually were one-sided, occurring over one eye or the other. She was nauseated during the attack but did not vomit. The bowels were costive.

Physical examination revealed an undernourished patient with evidences of gastroptosis.

The laboratory findings were: urine, normal; Wassermann reaction, negative; hemoglobin, 80 per cent.; red blood cells, 3,860,000; white blood cells, 4,700; blood sugar, 103 mg. per hundred cubic centimeters.

Fluoroscopic examination showed dilatation of the second and third portions of the duodenum; and the roentgen ray also showed an irregular constriction of the bulb which suggested the presence of adhesions to the gallbladder or liver. The lower pole of the stomach was just above the pubis.

A diagnosis of dilatation of the duodenum was made, and medical treatment, with diet, postural exercises and a corset, was begun, as the result of which the patient has improved slowly.

CASE 14.—A woman, aged 34, entered the clinic complaining of headache. There was a past history of scarlatina, pleurisy, and of an operation in which the tip of the coccyx had been removed. For two years the patient had had attacks of severe headache every month or so, with vomiting and a distressed feeling in the right side of the upper part of the abdomen. Between the

attacks there had been only slight abdominal pain. During the headaches she would vomit for one or two days. The bowels were costive; the appetite was good, the weight, stationary.

Examination revealed a tall, slim woman who appeared to be in poor health. The abdomen had a normal contour. The lower poles of both kidneys were palpable. A succussion splash was present over the stomach; there was a slight muscle spasm over the gallbladder, but no definite tenderness; a spastic sigmoid was palpable.

The laboratory findings were: urine, normal; Wassermann reaction, negative; blood, normal.

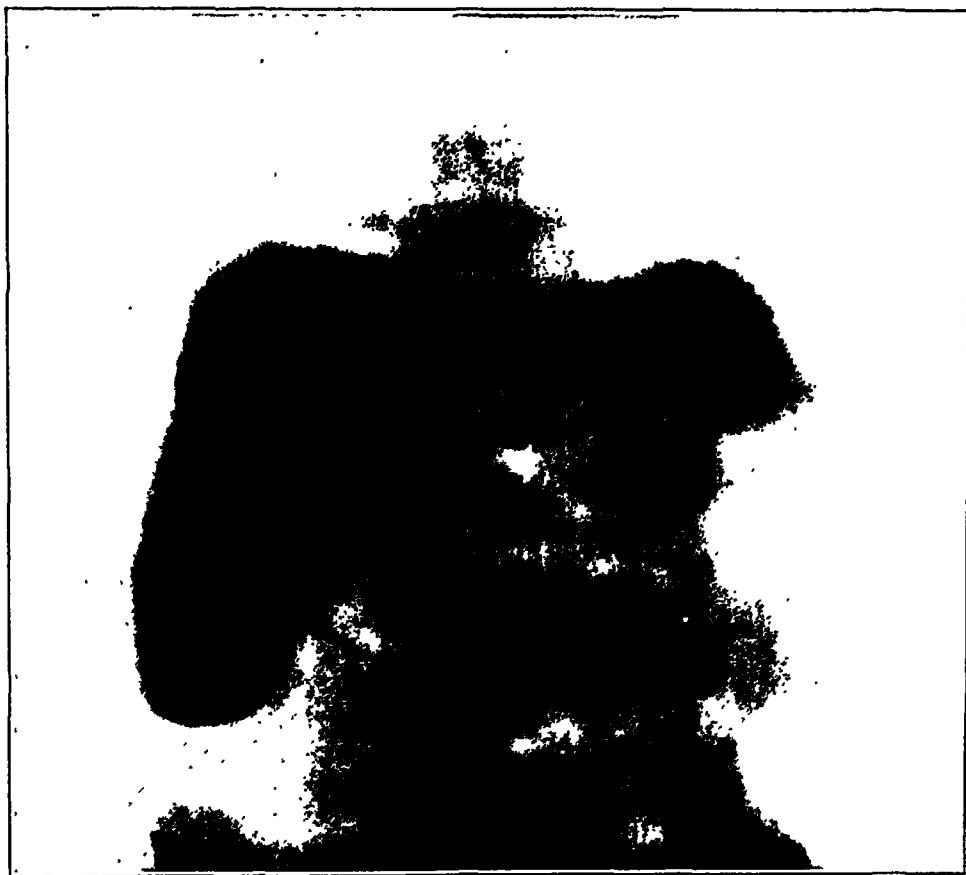


Fig. 4.—Megaduodenum (same case as shown in Figure 3).

The roentgen ray revealed a ptosed stomach, a normal duodenal bulb and an irregularly constricted and dilated duodenum with duodenal stasis.

For two years this patient has been under medical treatment for migraine, visceroptosis and chronic intestinal stasis with little improvement. This appears to be a classical case of duodenal dilatation, and I believe that complete relief of the headache, vomiting and pain would follow duodenojejunostomy.

CASE 15.—A man, aged 40, entered the hospital complaining of stomach trouble. He had had diphtheria when a child. For two years he had had intermittent attacks of stomach trouble, which were characterized by a burning sensation in the pit of the stomach associated with bloating from gas in the stomach and intestines; this occurred from two to four hours after meals

and occasionally at night. It was relieved by baking soda and food. He had had a skin eruption for months.

Examination revealed slight tenderness over the appendix and vague sensitiveness over the duodenal region.

The laboratory findings were: urine, normal; Wassermann reaction, negative; hemoglobin, 85 per cent.; red blood cells, 4,250,000; white blood cells, 8,700.

The roentgen ray showed a characteristic ulcer deformity (duodenal) with considerable dilatation of the descending duodenum.

The patient was placed on the medical regimen for duodenal ulcer. Four months later he was considerably improved and less deformity of the duodenal cap was present.

CASE 16.—A woman, aged 24, entered the clinic complaining of pain in the stomach, which she had experienced for two years. She had vague stomach symptoms, and was unable to eat anything with comfort on account of the formation of gas in the stomach. She had had influenza two years previously; her weight was stationary; there was no vomiting.

Physical examination showed nothing of significance except tenderness on deep pressure over the stomach.

The laboratory findings were normal.

The roentgen ray showed that the stomach and duodenal cap were normal, but there was marked ptosis with delay in the duodenum and reverse peristalsis.

Operation was advised but the patient wished medical treatment. She returned two years later complaining of an increase in the stomach symptoms, of occasional vomiting and of headaches. There had been no gain in weight; the bowels were regular. A strict medical regimen was again instituted with some resultant improvement.

CASE 17.—A man, aged 50, came to the clinic because of attacks of anorexia, nausea, epigastric distress and vomiting. There was a past history of syphilitic lesions and of a gonorrheal infection twenty-five years before, also of malaria and pleurisy. A cholecystectomy and appendectomy had been performed three years before. About fourteen years before he developed attacks of indigestion, which at first were severe and occurred at intervals; but for the last eight weeks he had had continuous epigastric distress with nausea and vomiting. No gallstone had been found at the previous operation, although a diagnosis of cholelithiasis had been made. He was losing weight and becoming weak, and had occasional attacks of transient vertigo. He was markedly constipated.

Examination revealed an emaciated, elderly man appearing worried and weak. A systolic murmur was present at the apex and transmitted to the axilla. The abdomen was scaphoid.

The laboratory findings were: urine, normal; Wassermann reaction, 4 plus; the colloidal gold test showed a tabetic curve; the blood picture was normal. Gastric analysis revealed: free acid, 1.5, total acid, 21.5.

Roentgen-ray examination showed dilatation of the duodenum with a deformity at the pyloric end of the stomach which was probably due to adhesions.

A diagnosis of tabetic crisis and dilatation of duodenum was made. Anti-syphilitic treatment was advised and a special diet, with the addition of hydrochloric acid.

CASE 18.—A man, aged 37, entered the clinic complaining of stomach trouble and headaches. An appendectomy had been performed four years

before. Headaches and stomach trouble began about fifteen years before, usually occurring when the patient was constipated. When the bowels had not moved for a day or two he would get dizzy and feel a thumping in the head; this terminated in a severe frontal headache which was not relieved until copious emesis had occurred. The vomitus at first consisted of food, but it continued after the stomach seemed to be empty, the later vomitus consisting of watery, bitter, green fluid. The attacks of vomiting lasted for from four to five hours. About an hour later the headache would begin to subside. The bowels were very costive. He had no abdominal pain, except occasional cramps.

Physical examination revealed a man of fairly healthy appearance. The abdomen was not distended, but there was generalized tenderness over the colon.

Laboratory findings were normal.

A roentgen-ray examination revealed dilatation of the duodenum, which was marked at the knee of the duodenum; there was a large diverticulum which held the barium twenty-four hours, and a deformity, evidently due to duodenal ulcer. The colon was generally spastic.

A diagnosis of duodenal ulcer, duodenal dilatation and diverticulum was made and medical treatment for the ulcer was instituted. An insufficient period of time has passed for any conclusions regarding the result.

CASE 19.—A woman, aged 29, entered the clinic complaining of hives. She had had an appendectomy twelve years before. The present trouble dated back two years when hives had appeared around the face and body. Later she had experienced considerable itching, and hives with welts appeared and have continued at intervals ever since. She had had frequent sick headaches with attacks of vomiting. The bowels were costive.

Examination was essentially negative except for the skin lesions and an infantile uterus.

The laboratory findings were: urine, normal; Wassermann reaction negative; hemoglobin, 85 per cent.; red blood cells, 4,550,000; white blood cells, 8,500; differential count, normal; blood sugar, 91 mg. per hundred cubic centimeters; blood urea, 39; blood uric acid, 2.2; serum calcium, 13.

The roentgen ray revealed dilatation of the second and third portions of the duodenum with high fixation of the bulb.

A diagnosis of urticaria, dilated duodenum and infantile uterus, was made, and medical treatment was instituted with some resultant relief.

CASE 20.—A woman, aged 49, entered the clinic complaining of stomach trouble and headaches. She had had typhoid fever at the age of 13. One year before the patient had had influenza. She complained of burning pain in the right side of the upper part of the abdomen and in the pit of stomach associated with nausea and vomiting. She was short of breath on exertion. The abdominal pain did not radiate. She had always been subject to sick headaches; her appetite was poor, and at this time she was on a diet. The bowels were very costive.

Examination revealed a thin woman, evidently in poor health; the abdomen was lax and doughy.

The laboratory findings were: urine, normal; hemoglobin, 80 per cent.; red blood cells, 4,660,000; white blood cells, 9,000.

Roentgen-ray examination showed dilatation of the second and third parts of the duodenum with temporary stasis.

Medical treatment was instituted with resultant improvement.

CASE 21.—A woman, aged 47, entered the clinic complaining of biliousness and liver trouble. She had had nausea and belching for years, and was usually constipated. One and one-half years and six months before she had had severe attacks of pain in the epigastrium and radiating to the back with very severe vomiting of bile stained fluid. Between these attacks she had considerable gas and nausea. The stools were light colored during the attacks. She had frequent headaches.

Physical examination revealed nothing of significance except for tenderness in the region of the gallbladder with the production of pain.

The laboratory findings were: urine, normal; Wassermann reaction, negative; hemoglobin, 85 per cent.; red blood cells, 4,130,000; white blood cells, 7,500.

The roentgen ray revealed dilatation of the duodenum, right-sided ptosis and dilated pelvic cecum. There was no evidence of any pathologic condition in the gallbladder.

Medical treatment for dilatation of the duodenum was instituted.

CASE 22.—A woman, aged 49, entered the clinic because of diabetes. She had previously had malaria. Diabetes was discovered one and one-half years before. Sugar did not appear in the urine after the patient was placed on a diet. She reentered the clinic because of the occurrence of pain in the stomach soon after eating, with palpitation and dyspnea. The stomach trouble began two weeks before. The bowels were costive.

Examination revealed a thin, sallow woman with a blood pressure of 110 systolic, 60 diastolic, and a definite, palpable thickening of the arteries. Tenderness was present in the region of the pylorus.

The laboratory findings were of little significance except for a blood sugar of 191 mg. per hundred cubic centimeters.

Roentgen-ray examination showed duodenal dilatation and kinking at the jejunal junction, which was evidently due to adhesions. The stomach and duodenal bulb were normal.

The patient was placed again under medical treatment for diabetes and treatment for dilatation of the duodenum was instituted with some resultant relief.

CASE 23.—A man, aged 40, entered the clinic complaining of stomach trouble. For some time he had felt nauseated in the mornings. He would feel better for an hour after breakfast, then would be distressed until noon, with relief again for an hour after the meal. He complained of considerable gas, but no vomiting. The bowels were very costive.

Examination showed the patient to be undernourished. His blood pressure was 120 systolic, 80 diastolic. There was slight abdominal tenderness.

The laboratory findings were: urine, normal; Wassermann reaction, negative; hemoglobin, 80 per cent.; red blood cells, 4,590,000; white blood cells, 7,900. Gastric analysis revealed: free acid, 7; total acid, 28.

Roentgen-ray examination showed a normal stomach and duodenal bulb, but antiperistalsis in the second and third parts of the duodenum. A diagnosis of chronic intestinal stasis with dilatation of the duodenum was made, and medical treatment was instituted with resultant improvement.

CASE 24.—A woman, aged 30, came into the clinic complaining of stomach trouble and skin lesions. An appendectomy had been performed two years before. She had always had stomach trouble, the worst feature of which was the persistent, almost constant daily vomiting of her meals. She had marked heartburn. For two years she had had pain in the epigastrium from two

to four hours after meals. The pain did not radiate. She would be awakened at night by the gastric distress. There had been no change in weight.

Examination revealed a healthy looking woman with a blood pressure of 105 systolic, 60 diastolic. There was generalized slight tenderness over the abdomen.

The laboratory findings were: urine, normal; Wassermann reaction, negative; hemoglobin, 85 per cent.; red blood cells, 4,290,000; white blood cells, 4,400.

Roentgen-ray examination revealed dilatation of the second and third portions of the duodenum; the stomach and bulb were normal.

A diagnosis of dilatation of the duodenum and possible gastric ulcer was made. Medical treatment was given with resultant improvement of the condition.



Fig. 5.—Dilatation of duodenum due to adhesions at duodenojejunal junction resulting from inflammatory mesenteric glands.

CASE 25.—A man, aged 43, entered the hospital complaining of stomach trouble. There was a past history of typhoid, malaria and pneumonia. He had had more or less stomach trouble for twenty years, consisting of bilious attacks with headaches and vomiting. His bowels were habitually constipated; the stools were pencil-like. When food was not taken he experienced a burning sensation in the epigastrium which was relieved by food or water. There had been no loss in weight.

Examination revealed a well developed man with sallow skin. The blood pressure was 106 systolic, 80 diastolic. The abdomen was rounded. There was tenderness below the left costal margin, and pressure over McBurney's

point produced pain referred to the former region. The sigmoid and descending colon were spastic.

The laboratory findings were: Wassermann reaction, negative; hemoglobin, 80 per cent.; red blood cells, 4,670,000; white blood cells, 6,300.

The roentgen ray revealed a moderate dilatation of the second and third portions of the duodenum suggesting duodenal stasis; the cecum was mobile; the appendix was not visualized.

Medical treatment for dilatation of the duodenum and constipation was instituted.

CASE 26.—A man, aged 25, entered the hospital complaining of pain and burning in the epigastrium. Four years before he had had deep jaundice, which was soon followed by pain in the upper abdomen. There had been no nausea or vomiting. His stools were clay colored. He had lost 10 pounds (4.5 kg.) in weight. He had had a slight jaundice for two years but this had entirely disappeared. Five weeks before he had developed a pain in the lower abdomen just below and to the right of the umbilicus. This shifted to the upper part of the abdomen and a sensation of burning not related to meals remained in the epigastrium. Soda seemed to give some relief. He sometimes had headaches.

Examination revealed a thin, apprehensive man of asthenic type, with a scaphoid abdomen and slight tenderness over the right side of the upper part of the abdomen.

The laboratory findings were: urine, normal; Wassermann reaction, negative; blood picture, normal.

The roentgen ray revealed a marked churning movement in the duodenum, which was slightly dilated. At times the barium was carried back into the bulb and stomach.

A diagnosis of dilatation of the duodenum was made and medical treatment was instituted.

CASE 27.—A woman, aged 24, entered the clinic complaining of pain in the lower part of the abdomen and of weakness with "dizzy spells." She had developed these symptoms since a miscarriage one year before. She was very weak and frequently obliged to go to bed. The pain at first had been in both sides but at this time was in the right side of the lower part of the abdomen. It had been worse during the preceding few days. She had a slight nausea, and was troubled with sour stomach and gas.

Examination revealed a fairly well nourished woman, with a blood pressure of 116 systolic, 70 diastolic. The right kidney was palpable. There was some gurgling in the region of the cecum and tenderness in the right lower quadrant. Vaginal examination revealed tenderness in the right adnexal region.

The laboratory findings were: urine, normal; Wassermann reaction, negative; hemoglobin, 75 per cent.; red blood cells, 4,010,000; white blood cells, 9,500.

Roentgen-ray examination showed a moderate dilatation of the duodenum with reverse peristalsis, and ptosis of the stomach.

A diagnosis of dilatation of the duodenum and salpingitis was made; medical treatment was instituted with resultant relief of the symptoms.

CASE 28.—A woman, aged 29, entered the clinic complaining of stomach trouble. She had had a previous appendectomy and an attack of influenza one year before, and since had had attacks of sour stomach and vomiting. She also was troubled with gas and belching. Her appetite was good. The bowels were costive.

Examination revealed a slight young woman with a blood pressure of 115 systolic, 75 diastolic. The abdomen was distended with gas.

The laboratory findings were: urine, normal; hemoglobin, 80 per cent.; red blood cells, 4,180,000; white blood cells, 7,600.

Roentgen-ray examination revealed distortion and dilatation of the descending duodenum and a distended colon.

Medical treatment was instituted with resultant improvement.

CASE 29.—A woman, aged 46, entered the clinic complaining of nausea. She gave a past history of bilious attacks for which cholecystectomy had been performed. She also had had an appendectomy and a right oophorectomy. She had had daily attacks of nausea for some years, starting each spring and lasting all summer. The nausea was present when she woke in the morning and tended to clear up by night. There was not much pain but some discomfort under the right scapula. She ate practically no food. The bowels were costive so that she took an enema every day. She had occasional headaches.

Examination revealed a short, obese woman with a blood pressure of 98 systolic, 70 diastolic. The liver edge was palpable.

The laboratory findings were: urine, normal; hemoglobin, 85 per cent.; red blood cells, 4,610,000; white blood cells, 9,200. Gastric analysis revealed: free acid, 0; total acid, 16.

The roentgen ray revealed that the descending duodenum was considerably elongated and that there was some stasis. A diagnosis of dilatation of the duodenum was made and medical treatment was instituted.

CASE 30.—A girl, aged 15 years, entered the hospital complaining of nausea, vomiting, weakness and loss of weight; she also had tachycardia. There was a past history of influenza. The patient had been in good health until one month before when she felt ill and began to vomit in the morning. Since that time she had had periods of nausea and vomiting. The vomitus was sour and consisted of the previous meal. She complained of weakness and had lost 16 pounds (7.3 kg.) in the preceding month. She had been given Lugol's solution with no resultant improvement.

Examination revealed a diffuse bilateral enlargement of the thyroid, but otherwise nothing of importance.

The laboratory findings were: urine, normal; hemoglobin, 85 per cent.; red blood cells, 4,710,000; white blood cells, 9,200; basal metabolism, plus 15. Gastric analysis revealed: free acid, 0; total acid, 25.

The roentgen ray showed a dilatation of the entire duodenum, and duodenal stasis was observed fluoroscopically. The stomach and duodenal bulb were normal. There was a moderate general resistance of the colon.

The patient was placed under medical treatment. The vomiting ceased while the patient was in the hospital and she was discharged. Two weeks later the father stated that she had had vomiting spells for two days, during each of which she would vomit five or six times. The vomiting was associated with a unilateral headache. This patient is to return later for a duodeno-jejunoscopy.

CASE 31.—A woman, aged 34, entered the clinic complaining of constipation and attacks of vomiting. She had been constipated for fifteen years. For the last four years she had had recurrent attacks of vomiting a few weeks apart. These attacks occurred when the bowels were sluggish. Early in the attacks she would get nauseated, and would finally vomit many times for days. She was losing in weight and had frequent headaches.

On examination the patient was found to be a small, slight woman with a blood pressure of 110 systolic, 60 diastolic. Slight tenderness was present over the cecum; spastic intestinal coils could be felt.

The laboratory findings were: urine, normal; hemoglobin, 80 per cent.; red blood cells, 4,520,000; white blood cells, 7,800; calcium, 8.

Roentgen-ray examination showed a moderately dilated but normal duodenal bulb held high in the right side of the hypochondrium. It was difficult under the fluoroscope to force barium from the bulb into the descending duodenum. The colon was atonic.

Diagnosis of gastric tetany and dilatation of the duodenum was made. Medical treatment was instituted and operation advised if relief was not secured.

CASE 32.—A woman, aged 27, in whom a diagnosis of globus hystericus had previously been made, returned to the clinic two years later complaining of frontal and temporal headache which was sharp and throbbing in character and was worse on exertion. She had no vomiting, but vertigo was usually associated with the headaches which were quite severe at times and necessitated immediate rest. These attacks were gradually getting worse.

Examination revealed a well developed and nourished woman, with a slightly enlarged thyroid gland but no increased activity.

The laboratory findings were normal.

Roentgen-ray examination revealed an undoubted moderate duodenal dilatation and duodenal stasis.

A diagnosis of dilatation of the duodenum was made. Medical treatment was recommended.

PATIENTS RECEIVING MEDICAL AND SURGICAL TREATMENT

CASE 33.—A woman, aged 21, entered Lakeside Hospital because of nausea and pain in the abdomen with vomiting and headaches.

Following an appendectomy four months previously she had gained 10 pounds (4.5 kg.) in weight; but the distress returned and she had pain 3 cm. above the umbilicus to both the left and the right of the midline. This occurred every day or so, soon after meals, especially after she had eaten a considerable amount. The pain lasted from one-half to one hour; there had been no vomiting recently but the nausea was persistent. She had previously vomited every morning soon after rising; the vomiting relieved the severe headaches that accompanied the attacks. Pain radiating to the left shoulder and back occurred occasionally at night. This was stabbing or cramping in character.

The only fact elicited by examination was a sharply defined area of tenderness the size of a dollar, 2 cm. above and to the left of the umbilicus, with some tenderness also in the right upper quadrant. The blood and urine were normal.

Roentgen-ray examination showed apparently delayed emptying of the duodenum with dilatation of the second portion. The fluoroscopic examination showed dilatation of the duodenum with incomplete and temporary obstruction of the third portion.

Medical therapy, consisting of a corset, postural exercises and diet, was instituted for six months. The symptoms were somewhat relieved but vomiting persisted. A duodenojejunoscopy was performed by Dr. Crile, at which the duodenum was found to be markedly dilated proximal to the point where it passed under the mesentery. Complete relief of symptoms has resulted.

CASE 34.—A man, aged 41, entered the clinic complaining of headaches and nausea. An appendectomy had been performed two years before, after which the same symptoms recurred. Pain referred to the shoulder-blades and accompanied by a sensation of fulness was present chiefly in the upper epigastrium. The bowels were costive. There was occasional nausea associated with severe headaches. The patient had lost 10 pounds (4.5 kg.) in the preceding four years.

Examination revealed an asthenic man with evidences of visceroptosis.

The laboratory findings were: urine, normal; hemoglobin, 80 per cent; red blood cells, 4,240,000; white blood cells, 6,100; Wassermann reaction, negative. Gastric analysis revealed: free acid, 38; total, 57.5; no bile or lactic acid.



Fig. 6.—Dilatation of duodenum due to adhesions caused by penetrating ulcer of lower curvature.

Roentgen-ray examination showed the stomach and duodenal bulb to be normal, but there was a large pouch just beyond the bulb.

A diagnosis of dilatation of the duodenum was made.

Medical treatment, consisting of a corset, postural exercises and diet, was instituted for one month with no relief.

An operation was then performed by Dr. G. W. Crile, at which the duodenum was found to be markedly dilated as the result of obstruction at the point where it crossed under the mesentery, which was very heavy; beyond this point no dilatation was seen.

A duodenojejunostomy was performed resulting in complete relief of symptoms.

CASE 35.—A woman, aged 47, entered the clinic complaining of constipation, headaches and vomiting. She had been constipated for years. She suffered from abdominal distress after meals and every two or three days had attacks of severe headache and nausea which were relieved by vomiting; she had frequent attacks of faintness. Her appetite was good but she was losing in weight.

The only points of importance elicited by the physical examination were that the patient was poorly nourished and pale; there was twitching of the upper and lower eyelids and a systolic murmur at the apex transmitted to the axilla, and there was some evidence of visceroptosis.

The laboratory findings were: urine, normal; Wassermann reaction, negative; hemoglobin, 80 per cent.; red blood cells, 4,308,000; white blood cells, 5,500.

Treatment by a support, postural exercises and a special diet was tried but the symptoms were not relieved and a later roentgen-ray examination showed that the cecum and ascending colon were very mobile, the hepatic flexure being at the level of the iliac crest.

At operation, which was performed by Dr. W. E. Lower, the last part of the first and second and third parts of the duodenum were found to be dilated to three times their normal size, owing to an obstruction at the point where the duodenum passed under the mesentery.

A gastro-enterostomy was performed, but only temporary improvement resulted and the patient will return for another operation.

PATIENTS RECEIVING SURGICAL TREATMENT ONLY

CASE 36.—A woman, aged 40, entered the hospital complaining of constipation and pain in the left upper portion of the abdomen.

Six years before she had suffered from an attack of acute indigestion and pain in the back which extended around to the heart. This pain was intermittent at first but had been more or less constant for the preceding four years. The bowels were costive; the appetite was poor, and regulation of the food was ineffectual. She had lost 10 pounds (4.5 kg.) in four years.

The blood and urine were normal and the Wassermann reaction was negative.

On examination diastasis of the recti muscles was marked. The lower pole of the right kidney was palpable and the entire kidney movable.

A diagnosis of chronic appendicitis was made, but at the operation, which was performed by Dr. G. W. Crile, the duodenum was found to be markedly dilated and ptosis of the stomach also was present. The duodenum passed under the mesentery, which was tight, and its vessels were dilated. A duodenojejunostomy and appendectomy were performed.

Four years later the patient reported that she had remained entirely well.

CASE 37.—A woman, aged 38, entered Lakeside Hospital complaining of attacks of pain in the epigastrium which were accompanied by severe headaches. For months she had been feeling unwell.

The only significant facts in the personal history were that she had had typhoid fever some years before, that her bowels were constipated, and that her weight was stationary.

The only findings of importance in the physical examination were enlargement of the thyroid, visceroptosis and a palpable right kidney.

The laboratory findings were normal. Roentgen-ray examination showed gastropsis and evidence of stasis in the duodenum which did not empty well.

A diagnosis of dilatation of the duodenum was made and an operation was performed by Dr. G. W. Crile, which confirmed the roentgen-ray findings of gastropsis and disclosed a greatly dilated duodenum with obstruction where the root of the mesentery crossed the duodenum.

Duodenojejunostomy and appendectomy relieved all the symptoms.

CASE 38.—A woman, aged 44, entered the clinic complaining of headache, weakness and vomiting. In the personal history the only point of interest was that she had had diphtheria. The present distress had first been noticed six months before. The attacks of vomiting had recently increased in frequency. Two months before she had fainted, and weakness had progressively increased. The headaches were severe but were relieved by the vomiting that occurred about one hour after meals. One month before she had experienced pain in the midepigastrium but this had subsided recently. She had been under medical treatment for the preceding six months.

Physical examination disclosed an anemic, poorly nourished woman. There were a few moist râles in the left apex of the lungs. The colon was palpable.

The laboratory findings showed albumin present in the urine; hemoglobin, 75 per cent.; red blood cells, 3,800,000; white blood cells, 5,400; differential count, normal; Wassermann reaction, negative. Gastric analysis revealed: free, hydrochloric acid, 50; total acidity, 82.

Roentgen-ray examination revealed a normal stomach, but the first portion of the duodenum was held toward the right suggesting the presence of adhesions. A diagnosis of dilatation of the duodenum was made.

At operation, which was performed by Dr. G. W. Crile, the duodenum was found to be dilated to two or three times its normal size from the pyloric end of the stomach to the point where it passed under the mesentery. The walls of the duodenum appeared to be atonic. Beyond the mesentery the intestines appeared normal.

A duodenojejunostomy was performed resulting in complete relief of symptoms.

CASE 39.—A woman, aged 55, entered the clinic complaining of pain in the epigastrium. About one year before pain had developed in the region of the gallbladder. The pain was intermittent, occurring at intervals of from two to three hours after meals. The temperature was sometimes elevated. Constipation was quite marked. The appetite was poor and there had been considerable loss of weight.

Physical examination revealed a thin, poorly nourished woman of sallow complexion. The abdomen was extremely flat and both kidneys were palpable.

The laboratory findings showed a secondary anemia.

An exploratory operation by Dr. G. W. Crile revealed a greatly dilated duodenum with a tight mesentery and adhesions about the gallbladder. The patient's condition became unfavorable during the operation and therefore the operation was limited to a narrowing of the lumen of the duodenum with silk sutures. One year later the patient was free from her former discomfort, but she complained of distention of the abdomen and of increasing constipation. Examination revealed a mass in the sigmoid flexure of the colon, which the operation showed to be an extensive carcinoma. In this case the original disturbance caused by the dilated duodenum was relieved by the plastic operation on the duodenum.

CASE 40.—A woman, aged 57, entered the clinic complaining of pain in the abdomen and vomiting. For the preceding three or four weeks the patient had had attacks of vomiting. The gallbladder, which was adherent to the duodenum

and contained stones, was removed. The second and third portions of the duodenum were found to be enormously dilated, and the question arose as to whether or not this was the cause of the vomiting. The patient was comfortable for two days following the operation and then began to vomit again. The vomiting, which was unaccompanied by pain, occurred at intervals of one or two days. By binding the abdomen and forcing the intestines upward, the vomiting seemed to be prevented and the patient was discharged from the hospital but was told to return if the vomiting recurred. Two months later she returned with a history of almost continuous vomiting for the preceding week with considerable loss of weight and strength.

Fluoroscopic examination showed the stomach in a low position, extending to the anterior superior spine. Bismuth passed into the duodenum where it stopped at the midline, ballooning out the duodenum to two or three times its normal size and then regurgitating back into the stomach. The roentgen-ray showed two fluid levels, one in the stomach and one in the duodenum in the obstructed third portion.

At operation, which was performed by Dr. H. G. Sloan, miliary tuberculosis was found to be present and also an enormous dilatation of the duodenum, which seemed to be compressed between the root of the mesentery and the spinal column. A duodenojejunostomy was performed. No vomiting followed the operation but four months later the patient died of Addison's disease.

CASE 41.—A man, aged 41, entered the clinic complaining of a dull pain across the back, violent headaches and a sensation of burning in the upper part of the abdomen. He had had a previous appendectomy. The foregoing symptoms had been present for ten years. At first they occurred every two or three months, lasting from four to six hours, until he vomited greenish yellow, bitter fluid. When he had vomited, the headaches would subside, but the pain in the back and the tenderness under the right costal margin would persist for two or three days. Recently the attacks had become more frequent. The bowels were costive.

Physical examination revealed at the apex a systolic murmur which was transmitted to the axilla. Over the gallbladder there was slight tenderness to deep palpation.

The laboratory findings were: urine, normal; Wassermann reaction, negative; hemoglobin, 85 per cent.; red blood cells, 3,997,000; white blood cells, 11,400; differential count, normal.

Roentgen-ray examination showed that the stomach and duodenal bulb were filled normally; but the fluoroscopic examination gave evidence of a moderate dilatation of the second and third portions of the duodenum.

At operation, which was performed by Dr. G. W. Crile, the pyloric ring was found to be dilated as were also the first and second parts of the duodenum, to the beginning of the third portion. The obstruction was produced by the mesentery as it passed over the third portion of the duodenum. A duodenojejunostomy was performed, and was followed by the complete disappearance of the symptoms.

CASE 42.—A woman, aged 28, entered the clinic complaining of pain in the abdomen. In 1918, seven years before, a gastro-enterostomy had been done for gastric ulcer; a plastic operation on the gastro-enterostomy for relief of obstruction was performed four years later, and a laporatomy for adhesions seven months after the plastic operation. During the seven years since the first operation the patient had had attacks of generalized abdominal distress, with severe headaches and vomiting, after taking solid foods or acids. Her

weight had been stationary, but her appearance was that of a poorly developed and undernourished woman.

The laboratory findings were: urine, normal; Wassermann reaction, negative; hemoglobin, 70 per cent.; red blood cells, 3,100,000; white blood cells, 7,800.

Roentgen-ray examination showed no barium passing through the gastro-enterostomy stoma. The second and third portions of the duodenum were dilated, and the lower pole of the stomach was at the level of the iliac crests.

At the exploratory operation performed by Dr. W. E. Lower, dense adhesions were found between the coils of intestines; the gastro-enterostomy



Fig. 7.—Dilatation of duodenum caused by mesenteric obstruction.

opening was patent; the duodenum was dilated with numerous adhesions about the third portion, and the mesentery was moderately tight.

The adhesions were severed by sharp dissection, but a duodenojejunostomy was not performed on account of the tendency to formation of adhesions. Nevertheless the condition of the patient improved.

CASE 43.—A man, aged 47, entered the clinic because of vomiting and headaches. For the last year he had had abdominal discomfort after meals and every few days during the last four months he had had attacks of severe headache and nausea, which were relieved by copious emesis. The bowels were costive. He had an eczema of the skin which was resistant to treatment.

Physical examination disclosed a few moist râles at the left apex.

The laboratory findings were normal. Roentgen-ray examination showed dilatation of the second and third parts of the duodenum.

At operation by Dr. G. W. Crile the duodenum was found to be dilated to two or three times its normal size, probably as the result of arteriomesenteric occlusion as the intestines appeared normal beyond that point. A duodenojejunostomy was performed and complete relief of symptoms followed.

CASE 44.—A woman, aged 26, came to the clinic complaining of metrorrhagia, headaches and vomiting. For years she had had postprandial attacks of epigastric distress with nausea, vomiting and belching, together with severe headaches which were relieved by copious emesis of bile stained fluid. During the preceding year she had had metrorrhagia and leukorrhea for which dilatation and curettage had been done five months before. The attacks of vomiting were more frequent during the menstrual periods, which were irregular. She was becoming progressively weaker.

On examination tenderness to pressure was found to be present over the entire abdomen but chiefly in the right iliac fossa.

The laboratory findings were normal. Roentgen-ray examination showed duodenal stasis and gastropnoxis with atony. The second and third portions of the duodenum showed dilatation with stasis. There was vigorous peristalsis and the stomach was dilated and atonic, its lower pole being 5 inches (12.7 cm.) below the iliac crests.

Operation by Dr. T. E. Jones disclosed a dilatation of the second and third portions of the duodenum which was caused by arteriomesenteric occlusion. A duodenojejunostomy was performed and complete relief of symptoms followed.

CASE 45.—A woman, aged 26, entered the clinic complaining of abdominal pain and distress after meals. One year before she had been operated on for appendicitis but the symptoms had returned. The pain, which was in the epigastric region and occurred soon after meals, was sometimes very severe and was relieved only by the vomiting of bile stained, sour fluid. Her diet was modified but to no avail.

Laboratory findings revealed normal blood and urine.

An exploratory laparotomy was performed by Dr. H. G. Sloan, at which the duodenum was found to be dilated to three times its normal size. On slipping the finger under the superior mesenteric artery a definite tightness and tugging could be demonstrated.

A duodenojejunostomy was performed, and was followed by relief of symptoms.

CASE 46.—A woman, aged 63, entered the clinic complaining of pain in the right side of the abdomen with fever, loss of weight, weakness and constipation. She had been apparently well until one year before, when she became aware of an occasional dull aching pain in the right side of the abdomen with flatulence and sour stomach. She had increasing constipation and her appetite was poor.

Two months before she had been kept in bed for two days by a sharp attack of pain in the right side, with the appearance of a lump in the upper abdomen. This attack was accompanied by an elevation of temperature. The lump disappeared after copious emesis. For weeks after this attack she had occasional distress, and later another attack similar in character to the first; the swelling as before disappeared after vomiting. The bowels were costive.

Physical examination revealed an emaciated, poorly developed woman. The abdomen was thin walled, was flat and freely movable. There was a palpable tender swelling in the right upper quadrant.

The blood and urinary findings were normal.

The diagnosis of cholecystitis was made. At operation by Dr. G. W. Crile a large dilated duodenum was found. The patient's pulse became poor and the operation was confined to a narrowing of the lumen of the duodenum by blocking it with silk sutures.

The symptoms disappeared but one year later the patient returned and an extensive carcinoma of the sigmoid was found at an exploratory operation by Dr. Crile. No later report has been secured.

CASE 47.—A man, aged 40, came to the clinic because of pain and a sensation of burning in the epigastrium. These symptoms had first appeared eighteen years before, at which time a diagnosis of cholelithiasis had been made. At operation no pathologic condition of the gallbladder had been found; at that

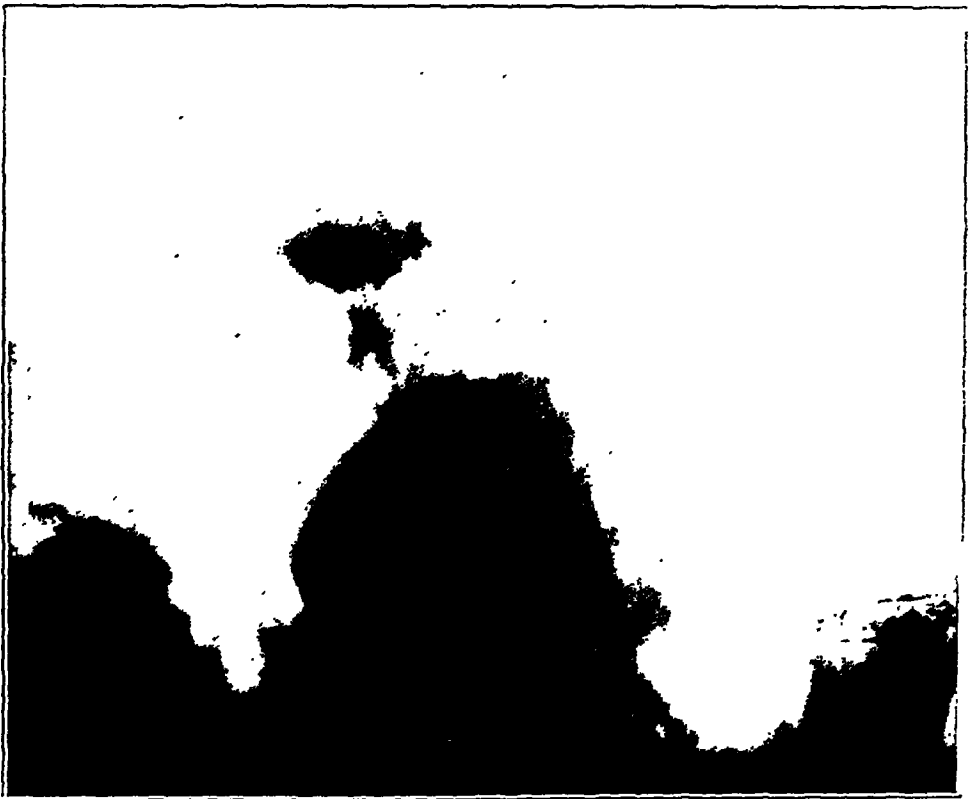


Fig. 8.—Dilatation of duodenum caused by mesenteric obstruction.

time the appendix had been removed. The same symptoms recurred and persisted for eight years when a gastro-enterostomy was done with no resultant relief. The pain and burning had recurred, and he continued to have occasional spells of vomiting. The bowels were costive. A diagnosis of a vicious circle was made.

The physical examination revealed an anemic, pale man; the abdomen was scaphoid but showed no tenderness to palpation.

Laboratory findings revealed normal urine, but the blood showed a secondary anemia.

At operation by Dr. G. W. Crile, the duodenum was found to be markedly dilated to almost the size of the stomach and the gastro-enterostomy opening was practically closed by adhesions. After the adhesions had been severed by

sharp dissection the opening was found to admit three fingers. The enlarged lumen of the duodenum was narrowed by blocking the canal with interrupted silk sutures.

The patient's condition improved.

CASE 48.—A woman, aged 30, entered the clinic complaining of pain in the abdomen. For thirteen years she had had pain in the abdomen, radiating to the intrascapular region, which she attributed to a strain from mountain climbing. The pain was not accompanied by nausea or vomiting. The bowels were very costive. She had frequent severe attacks of headache. Examination revealed a poorly nourished, asthenic woman with rather a yellowish tint to the skin; the abdominal wall was lax, and there were evidences of gastropotosis. The blood and urine were normal.

Roentgen-ray examination revealed gastropotosis and delayed emptying of the duodenum.

Dr. G. W. Crile performed a duodenojejunosomy and appendectomy and complete relief of symptoms resulted.

CASE 49.—A woman, aged 29, entered the clinic complaining of distention of the abdomen and vomiting which had lasted for one year. The ankles were considerably swollen and the eyes were puffy. She had occasional severe headaches, which were followed and relieved by copious emesis which gave evidence of stasis (fluid or food was retained for ten hours). The vomitus was bile stained. Occasionally she had pain in the abdomen. During the preceding ten weeks she had lost in weight from 125 to 114 pounds (56.7 to 51.7 kg.). The bowels were costive.

Examination revealed an anemic, undernourished woman, with evidence of gastropotosis. A splashing sound was elicited by pressure above the umbilicus.

Roentgen-ray examination showed coloptosis and gastropotosis and gave evidence of duodenal stasis with dilatation of the bulb and of the first and second portions of the duodenum. The laboratory findings were: urine, normal; Wassermann reaction, negative; hemoglobin, 85 per cent.; red blood cells, 4,024,000; white blood cells, 5,400; differential count, normal. Gastric analysis revealed: free acid, 36; total acid, 59.

At operation by Dr. G. W. Crile, it was found that the dilatation stopped abruptly where the duodenum passed under the root of the mesentery. A duodenojejunosomy was performed and complete relief of symptoms followed.

CASE 50.—A man, aged 45, entered the clinic complaining of headaches and vomiting. A past history of two attacks of typhoid fever at the ages of 15 and 35 years, respectively, was elicited. He had had recurrent headaches almost all his life. These had recently been less severe but more frequent. These headaches were usually in the region of one temple or the other, and lasted from twelve hours to from one to three days. He was nauseated and frequently vomited, with resultant relief of the headache.

The case was diagnosed as migraine and was treated medically with diet and luminal, but the symptoms persisted for the following two years when the patient came to the clinic.

Physical examination failed to elicit any important points.

The laboratory findings were: urine, normal; Wassermann reaction, negative; hemoglobin, 80 per cent.; red blood cells, 3,470,000; white blood cells, 5,700; differential count, normal.

Roentgen-ray examination showed duodenal stasis and dilatation of the second and third parts of the duodenum.

At operation by Dr. T. E. Jones the duodenum was found to be markedly dilated, and the pylorus was open admitting two or three fingers. It was evident that mesenteric obstruction was the cause of the dilatation. A duodenojejunostomy was performed and complete relief resulted.

CASE 51.—A woman, aged 30, entered the clinic complaining of sick headaches and goiter. She stated that for sixteen years she had been subject to sick headaches accompanied by vomiting, the vomitus being dark green. The headaches occurred usually in the morning and were relieved by the vomiting, which usually occurred about noon. The bowels were costive.

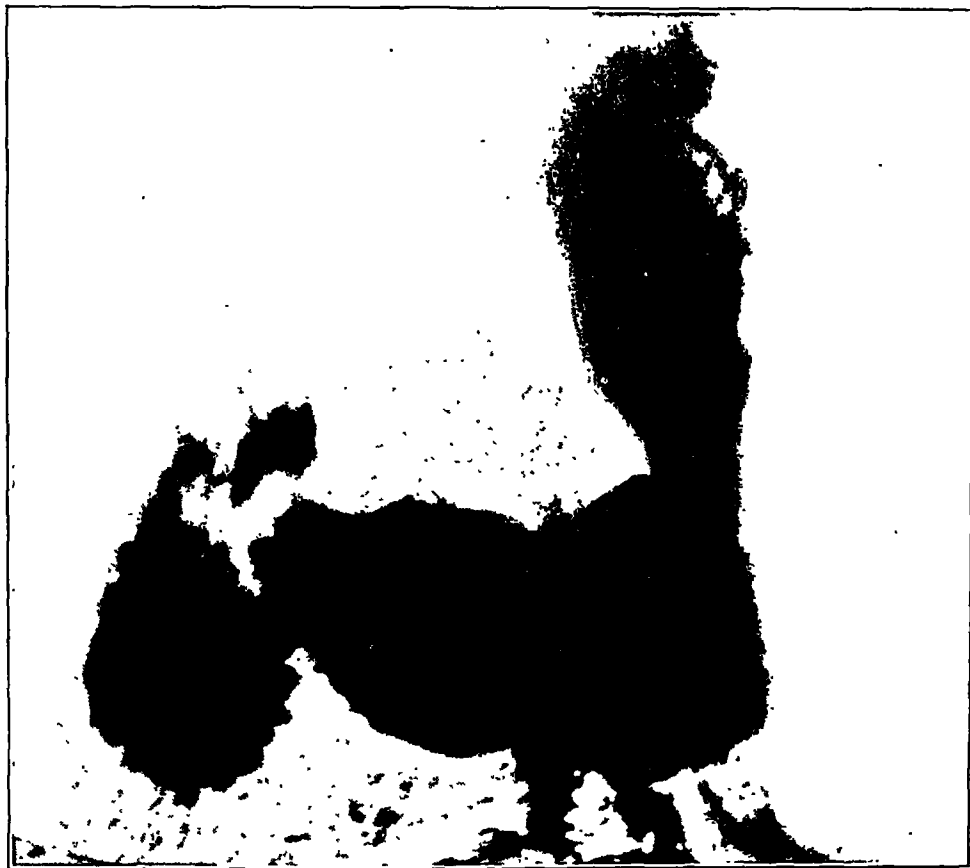


Fig. 9.—Dilatation of duodenum with duodenal ulcer.

The only significant points disclosed by physical examination were a colloid goiter and evidence of visceroptosis.

The laboratory findings were: urine, normal; Wassermann reaction, negative; hemoglobin, 90 per cent.; red blood cells, 4,020,000; white blood cells, 8,300.

Roentgen-ray examination showed an elongated and dilated descending duodenum with antiperistalsis. The stomach and duodenal bulb were normal.

At operation by Dr. G. W. Crile, the duodenum was found to be dilated as far as the point where it passed under the mesentery; from there on it appeared to be normal.

A duodenojejunostomy was performed, and freedom from symptoms resulted.

CASE 52.—A man, aged 31, entered the clinic complaining of headaches and vomiting. There was a past history of pneumonia and pleurisy. For sixteen years he had had attacks of headache, with nausea and vomiting, which had become progressively worse and more frequent until he was experiencing them from four to six times a month. The attacks began with pain over each temple followed by nausea and vomiting. A diagnosis of migraine had been made, medical treatment for which had failed to give relief.

Physical examination was negative except for evidences of gastropnoxis and colopnoxis. The laboratory findings were normal. Roentgen-ray examination revealed dilatation of the second and third portions of the duodenum and 25 per cent. retention in the stomach after four hours.

At operation by Dr. G. W. Crile the duodenum was found to be dilated and obstructed at the point where the duodenum passed under the mesentery. A duodenojejunosomy was done, and an immediate relief of symptoms resulted, but the interval of time since operation has been too brief to warrant definite conclusions as to the permanency of the cure.

CASE 53.—A man, aged 42, entered the clinic complaining of abdominal pain, vomiting and loss of weight. He gave a past history of typhoid fever at the age of 14, appendectomy seven years before, and of a plastic operation for duodenal ulcer four years before. For three years after the last of these operations he had no trouble, as he adhered to a fairly strict diet. During the preceding year, however, the patient had vomited at intervals, sometimes twice daily and sometimes only once a week. There was slight pain before emesis. He had lost 12 pounds (5.4 kg.) in weight. The vomiting was becoming progressively worse. The bowels were costive.

Examination revealed a poorly developed, rather emaciated man with a blood pressure of 90 systolic, 60 diastolic. The abdomen was scaphoid. Palpation was unsatisfactory.

The laboratory findings were: urine, normal; Wassermann reaction, negative; hemoglobin, 85 per cent.; red blood cells, 4,340,000; white blood cells, 11,000.

Roentgen-ray examination showed the niche of a penetrating ulcer on the lesser curvature in the media of the stomach, and very much dilated second and third portions of the duodenum which suggested the presence of adhesions that had caused stenosis of the distal duodenum.

Dr. W. E. Lower resected the lower portion of the stomach containing the ulcer and performed a gastro-enterostomy (Billroth II).

The ulcer was considered to be the major pathologic condition in the case, accounting for the type of surgical procedure.

Twenty days later the patient was free from symptoms. This case is also too recent to permit conclusions as to the permanency of the cure.

CASE 54.—A man, aged 38, entered the hospital complaining of pain in the abdomen. He had had a previous gastro-enterostomy and appendectomy following which he had had occasional attacks of pain. For five years he had had a dull throbbing pain in the right side. He had attacks of vomiting and headaches at intervals with attacks of cramps in the stomach and soreness and pain after meals. The bowels were costive.

Examination revealed a fairly well developed man with evidences of gastropnoxis. There was tenderness to palpation in the region of the pylorus.

The laboratory findings were: urine, normal; Wassermann reaction, negative; blood, normal.

Roentgen-ray examination showed that some barium passed by way of the pylorus, a distorted duodenal bulb and stasis at the knee of the second and third parts of the duodenum. There was from 25 to 30 per cent. retention in the stomach, a dilated duodenum and jejunum in five hours.

At operation by Dr. G. W. Crile the jejunum also was found to be dilated. A resection of the previous gastro-enterostomy with an end-to-end anastomosis of the jejunum was performed, and the patient was discharged from the hospital in an improved condition.

CASE 55.—A woman, aged 42, entered the clinic because of headaches and attacks of pain in the right upper quadrant of the abdomen with vomiting. She had suffered from these attacks for years. An appendectomy, a cholecystostomy, a cholecystectomy, and severance of adhesions to the common duct had been performed but without giving her any relief. The attacks had increased in frequency and seemed to occur in cycles of two weeks. During the attacks the patient vomited the contents of the stomach followed by a considerable amount of bitter, dark bile. During the attacks she sometimes experienced severe pain in the region of the gallbladder, radiating to the back and right scapula. The headaches were frontal in type, dull aching in character and were relieved by vomiting. There had been a slight loss in weight.

Examination revealed a well developed woman, slightly anemic.

The laboratory findings were normal.

Roentgen-ray examination revealed a marked dilatation of the duodenum with stasis. The stomach and duodenal bulb were normal.

This patient is to return later for duodenojejunostomy. She has been operated on five times without any relief from symptoms. I believe the correct diagnosis has now been established and that the duodenojejunostomy will result in a cure.

CASE 56.—A man, aged 35, entered the clinic complaining of burning pain in the stomach for the relief of which an appendectomy had been performed ten years before but without avail. Since that time the distress had recurred at intervals and recently had been more or less constant and was sometimes accompanied by headaches and nausea; occasionally he had dizzy spells. A diagnosis of duodenal ulcer had been made and the patient had been put on a Sippy diet without relief.

Physical examination revealed an undernourished man. The abdominal wall was flaccid and the transverse colon was palpable; some tenderness was felt over the gallbladder.

The laboratory findings were: urine, normal; hemoglobin, 80 per cent.; red blood cells, 4,490,000; white blood cells, 6,800. Gastric analysis revealed: total acidity, 27.5; free hydrochloric acid, 10.5.

Roentgen-ray examination showed a dilated bulb and duodenum; the stomach was normal.

A diagnosis of dilatation of the duodenum was made and a duodenojejunostomy performed with complete relief of symptoms.

CASE 57.—A man, aged 42, entered the clinic complaining of nervousness, weakness and loss in weight. There was a past history of typhoid and pneumonia. The appetite was fair, and he had no gastric symptoms except for gas in the intestines. The bowels moved fairly well. He had occasional attacks of diarrhea, but never any blood or mucus in the stools.

Examination revealed palpable masses in the colon which felt like fecal material. The blood pressure was 104 systolic, 80 diastolic.

The laboratory findings were: urine, normal; Wassermann reaction, negative; phenolsulphonephthalein, 52 per cent. in two hours; hemoglobin, 80 per cent.; red blood cells, 4,750,000; white blood cells, 7,800; differential count, normal.

Roentgen-ray examination revealed an irregular constriction and dilatation of the second and third portion of the duodenum. The stomach and duodenal bulb were normal, the cecum mobile and the ascending colon ptosed.

A diagnosis of dilatation of the duodenum was made and operation advised. The patient is to return later

PUNCTURE WOUNDS OF THE CEREBELLUM

INJURY OF CEREBELLUM BY FOREIGN BODY ENTERING THROUGH JUGULAR FORAMEN, WITH REMOVAL AND RECOVERY

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In this day when one hardly dares submit a clinical report unless it is based on a large experience and is authoritative and acceptable from numerical vastness, if from nothing else, one cannot feel justified in detailing his clinical experiences with a "series of one case" unless that case is sufficiently extraordinary to be of unusual interest.

Puncture wounds of the cerebellum are common enough, especially in time of war, but a penetrating wound of the cerebellum from an object entering the jugular foramen by way of the mouth is an extremely rare injury, while deep puncture of the cerebellum by a foreign body by this route, with removal of the body followed by recovery of the patient, is so unusual that the occurrence of such a case seems worthy of report. I find no similar example in the literature of recent years while a search through fifty older articles carrying general titles but touching on cerebellar injuries failed to reveal one.

Huppert¹ says concerning the penetration of the cerebellum by a foreign body, whether extracted or not, that the result is almost invariably fatal. In fact, this was the usual testimony, at least prior to the Great War; hence, it is exceedingly remarkable that a person should have survived a deep puncture of a cerebellar lobe when the object was a large and blunt one and when that object entered through the jugular foramen. Necessarily it was in the closest proximity to structures of no less importance than the ninth, tenth and eleventh cranial nerves, the inferior petrosal sinus, the lateral sinus, and the meningeal branches from the ascending pharyngeal and occipital arteries. Such a patient has recently been under my observation.

I was inclined seriously to question the possibility of such an injury as that interpreted by the roentgenologist, who telephoned his diagnosis to me, and was unconvinced until I had examined the plates and, later, the patient. That the object had traversed the lateral wall of the pharynx, had entered the jugular foramen, and had penetrated the left cerebellar hemisphere to a depth of 5 cm. could not be questioned.

REPORT OF CASE

History.—S. H., a boy, aged 2½ years, was admitted to the hospital on the evening of March 28, 1923. The mother said that about one hour before the child, while running with a double ended ivory crochet hook in its mouth,

1. Huppert: Arch. f. Heilk. Berl. 6, 1875.

tripped, fell forward on his face and immediately began violently coughing and vomiting. In a moment or two he coughed out one-half the hook, which had broken at its center, and, as the remainder could not be found, it was supposed that it had been swallowed or insufflated. The child, although fully conscious, seemed totally unable to talk or cry. For a few minutes there was slight bleeding from the nose. The patient was at once placed in an automobile and sent to the hospital, some fifteen miles distant.

Physical Examination.—The patient was well nourished and developed. He lay quietly on the cot, occasionally coughing and vomiting. He neither talked nor cried, and seemed unable to do either. The pulse was 110, the temperature normal, the respirations slightly hurried and accompanied by a wheezing inspiratory stridor. There was a large quantity of mucus and vomitus in the mouth and throat, which the patient seemed unable to expel. On its removal and on examination of the mouth and pharynx, no lacerations were discovered and no sign of the missing crochet hook. The general physical examination, hurriedly made at this time, was negative.

The patient was immediately examined fluoroscopically with the full expectation of finding the missing object in the upper air passages or in the alimentary tract. No evidences of it were found in the abdomen or in the thorax. It was almost by accident that the screen was moved over the child's head revealing the metal end of the hook in the upper pharynx, and, on lateral view, it was found to project into the left cerebellar hemisphere for nearly its entire length. Steroscopic plates were made, immediately developed, and the hook definitely localized in the brain.

The patient was at once prepared for operation. Since nitrous oxid caused profound cyanosis, it was discarded for ether, but even then with only partial success. With the aid of mouth gag and head mirror a tiny punctured wound was found in the upper portion of the left anterior tonsillar pillar through which a probe could be passed for 5 or 6 cm., at which point it came into contact with the metal screw on the end of the lost crochet hook. It was necessary to incise the tract so as to admit forceps, several of which were tried before a satisfactory one was found. Finally, a long Hagar needle holder being used, the screw on the end of the ivory hook was grasped, and, with a slight rotating motion, the hook removed. The object was firmly fixed, and a surprising amount of traction had to be used before it could be loosened. When it finally came away there was a sudden and profuse hemorrhage from the wound which was at once controlled by a long iodoform gauze pack. The child's respirations at once ceased. For ten minutes artificial respiration had to be resorted to, after which period the patient began to breathe again; in a few minutes he was breathing naturally.

When the patient returned from the operating room his temperature was 97 degrees, pulse 120, and respirations 50. That night the patient vomited slightly and coughed occasionally. Extreme restlessness was finally controlled by codein. On the following day the pack was removed. Twenty-four hours after the operation the left eyelids became slightly swollen, and, at the same time, the left ear became discolored. During the first few days there were wide fluctuations in the temperature but by the ninth day both temperature and pulse were normal. Following the operation, and until the patient left the hospital, thirteen days later, he experienced great difficulty in swallowing, much of the liquid food returning through the nose. There were no urinary changes other than an increase in the specific gravity, and no glycosuria (Claude Bernard).

The second day the eye grounds were negative and neither strabismus nor nystagmus were present. The child lay quietly in bed, and, except for great difficulty in swallowing, seemed quite normal. There apparently was no involvement of the facial nerve and no changes in the reflexes.

The fourth day the patient had difficulty in swallowing. The food regurgitated through the nose. Talking was difficult. Apparently there were no visual disturbances.

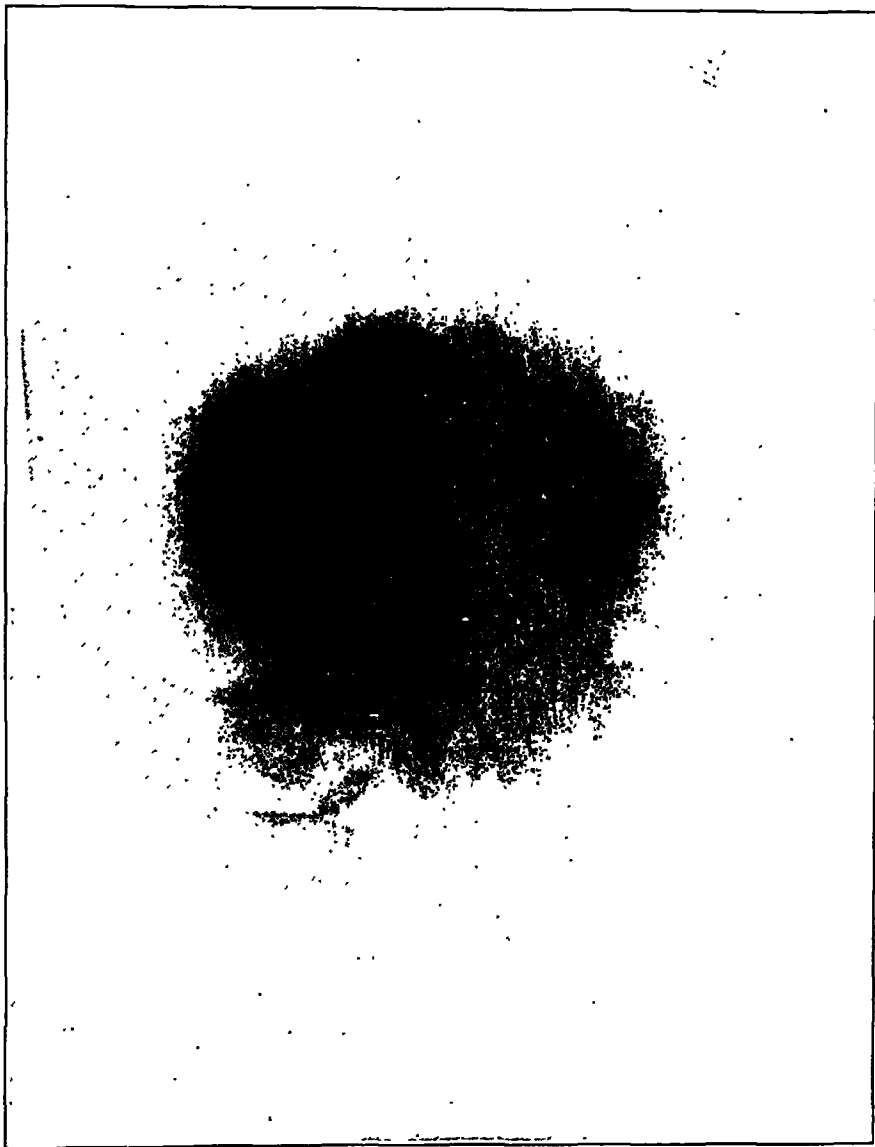


Fig. 1.—Anteroposterior view within an hour of the accident, showing shadow of handle of crochet hook with steel screw.

The fifth day the patient was out of bed. There was a tendency for the child to fall to the left when walking, and it was impossible for him to walk in a straight line. He swallowed better with no regurgitation through the nose. At no time were there evidences of meningitis.

The sixth day the ataxia was less pronounced but the patient still displayed some tendency to fall to the left, these being the only signs of dysmetria or

asynnergia exhibited. He talked better and swallowed much better. At no time were there convulsions.

The thirteenth day the patient was discharged. He still showed a slight tendency to veer to the left and had some difficulty in swallowing.

For five or six weeks after returning home the child experienced slight difficulty in swallowing. The mother was obliged, therefore, to be cautious in selecting his food. Solids could be taken only with great difficulty for on such occasions the patient would "choke up" and regurgitate froth and mucus. For several weeks speech was impaired but it finally became normal. For a long time the patient talked only in a whisper.

He was reexamined, November 29, ten months following the injury, at which time the patient seemed normal in every particular.

I reported the case to several neurologists, who have kindly permitted me to add their comments to this paper.

DR. WILLIAM G. SPILLER: The case you describe in your letter is one of exceptional interest. It is remarkable that the child had no hemorrhage and had so little reaction. The course of the crochet hook seems to indicate that the foreign body passed to one side of the medulla oblongata, and thus escaped injuring vital structures. The great danger now is from infection, and if it escapes this, there may not be any serious symptoms. The point of entrance into the skull was through the jugular foramen, and yet the hook avoided the inferior petrosal sinus, the lateral sinus, the meningeal arteries, and the ninth, tenth and eleventh nerves. The facial and acoustic nerves were not far away. It is difficult to examine all these nerves in a young child, and there may be some injury which cannot be detected at present.

DR. F. X. DERCUM: I am greatly interested in the very remarkable case which you describe. Like yourself, I know of no similar case. Both the accident and the outcome are most extraordinary. It seems almost impossible that the inferior petrosal sinus and the lateral sinus or the glossopharyngeal and spinal accessory nerves should have escaped. Of course the difficulty in swallowing and regurgitation might be accounted for by injury of the glossopharyngeal, but this, according to the history, seems not to have been serious in nature, for the symptoms early disappeared. You no doubt examined the child for hemiasynnergia, dysmetria, adiadokokinesis and allied symptoms, and, if they were absent, this would confirm the view that the injury of the cerebellum was limited to the lateral lobe.

Subsequently, he wrote: I have examined your plates and there can be no doubt as to the position occupied by the crochet needle and I cannot but again express my amazement at the recovery. I am returning the plates by this mail. I feel under great obligations to you for permitting me to see them. I trust that you will now publish your paper without further delay.

DR. WALTER E. DANDY: Your case is indeed an interesting one. It was certainly a far-seeing needle to have ever been able to find the jugular foramen. I wonder if the child had convulsions either at that time or subsequently. There is no reason why it should have had them, but it would be very interesting to know that it did not. There are, of course, many cases of foreign bodies, but none that I know that entered through the jugular foramen.

DR. CHARLES A. ELSBERG: The case you describe in your letter is certainly a very interesting one and a most unusual accident. I have never seen nor heard of an injury of this kind. I have, however, seen a child who fell with a buttonhook in its mouth and sustained a puncture wound of the nasopharynx with a perforation into the cranial cavity. When I saw the child, she had the

signs of a meningitis to which she rapidly succumbed. I think the result you obtained in your remarkable case is an excellent one.

DR. C. H. FRAZIER: I have read with much interest the account of the puncture wound of the left cerebellar hemisphere. So far as I can recall, we have no record of an injury of that nature. Of course the attacks of respiratory failure associated with lesions of the posterior fossa, and particularly cerebellar tumor, have been observed often and, as you no doubt know, in some cases life has been prolonged by artificial respiration from eighteen to twenty hours. That is, the patient survived eighteen hours or more after voluntary respiration had been wholly lost. Recovery in your case is extremely gratifying.



Fig. 2.—Lateral view within an hour of accident, showing shadow of crochet hook in jugular foramen and cerebellar fossa.

DR. A. W. ADSON: I have never personally had a case of this kind and, off hand, I do not recall having heard of one. I think that it would be well worth while to go into the case fully and report it.

DR. HARVEY CUSHING: I am glad to have the details of this extraordinary case. I am quite sure that I have seen records of similar episodes, and it is an old wives' caution for children that they must not run about with sharp pencils or scissors in their hands lest they get their brains punctured. However, that the weapon should be a crochet needle and that it should go through the jugular foramen is such an unusual combination of circumstances as to justify a clinical report of the case.

PHYSIOLOGY OF CEREBELLUM

Although our knowledge of cerebellar physiology is extremely limited, we do know that severe injuries of the cerebellum produce certain phenomena, known collectively as the "cerebellar syndrome," consisting chiefly of ataxia, the component parts of which are: dysmetria, a term used to designate disturbances in the performance of voluntary movements; asynergia, or lack of synchronization, and adiadokokinesis, an inability to execute voluntary movements successively and rapidly.

In some way the cerebellum exerts a regulatory influence on the nervous mechanism, thus controlling voluntary movements, and we may

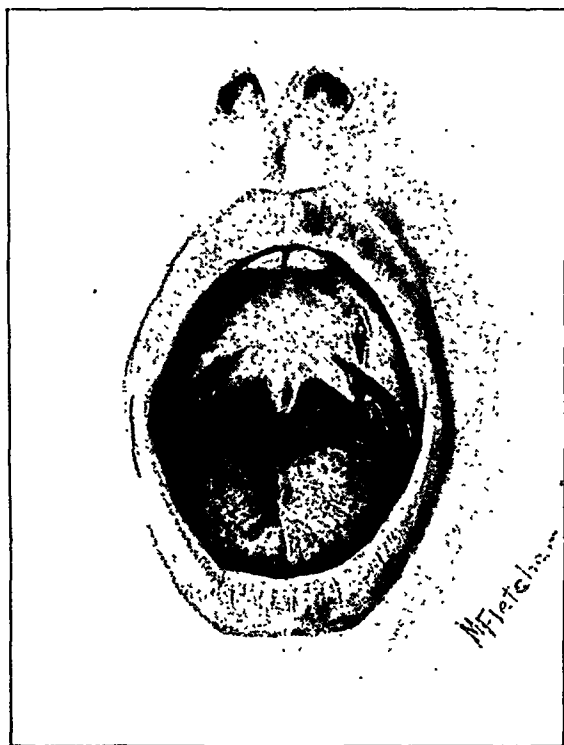


Fig. 3.—Position of wound of entrance in left anterior tonsillar pillars.

accept the original idea of Flourens (1824) that the organ is a coordinating center for the complex voluntary movements utilized in producing locomotion and in maintaining equilibrium.

Cerebellar influence on body musculature is homolateral; that is, each hemisphere is associated with its own half of the body; while its connection with the motor area of the cerebrum is just the reverse, the right cerebral hemisphere being in relation with the left half of the cerebellum. The degrees of consciousness shown by the small brain is slight, or, at least, of a much lower order than that of the cerebrum, since experimental removal of the cerebellum produces no apparent loss of sensation (Howell).

In animals, experimental removal of all or part of the cerebellum produces no striking evidences of muscular paralysis, but, instead, a curious lack of power to coordinate properly the contractions of the various muscles involved in the maintenance of equilibrium. Following cerebellar resection pigeons are unable to fly, and they walk with a staggering, drunken gait, a condition designated as cerebellar ataxia.

Unilateral operations on the cerebellum of mammals give somewhat similar results. If one hemisphere is resected, there is a tendency to forced movements directed toward the injured side, a turning or rotation of the body to left or right.

In human beings afflicted with cerebellar atrophy or neoplasm, the fundamental symptom is lack of accurate coordination, as manifested by an ataxic gait and lack of skill in performing definite movements that require the associated activity of several muscles.

A review of the more notable case reports in the literature of cerebral and cerebellar traumatism by puncturing objects may at this time be of interest.

Slee:² A plumber, aged about 30, was shot in the abdomen and thigh; he was operated on and death followed two days later from general septic peritonitis. Necropsy, Feb. 15, 1890, revealed a knife blade $\frac{5}{16}$ inch wide penetrating 1 inch (2.5 cm.) into the left occipital lobe. The point of the blade was ensheathed in a strong fibrous capsule; there was no depressed or displaced bone; the blade was black, corroded and showed signs of having been in position for years. Inquiry showed that the man's family had never known of an injury that had caused cerebral or other symptoms during life.

Delanglade:³ A man, aged 17, fell from a ladder a distance of 2.5 meters: an open knife held in the hand penetrated 4 cm. into the frontal lobe and 3 cm. above the orbital margin. The knife blade was extracted by traction in the direct axis of the blade. There were no hemorrhages, and no sutures were taken. Treatment was given with compresses, and recovery followed in twelve days. No after symptoms were noted and no injury to the eye except a slight degree of ptosis.

Vallas:⁴ A man, a mason, had a stone weighing 2 kg. fall on his head; a few days later he suffered the onset of jacksonian epilepsy and right hemiplegia. Physical examination revealed a 2 cm. long knife blade in the left side of the brain. Extraction of the blade was followed by death two days later from diffuse meningitis. Necropsy showed that a blade had pierced the paracentral lobe. Inquiry revealed that a knife blade had been in the brain for two years as the result of a brawl, but that it had caused no cerebral symptoms.

Kennedy:⁵ A boy, aged $3\frac{1}{2}$ years, while wearing a straw hat, fell on an iron spike which penetrated the head 1 inch (2.5 cm.) above the right ear and car-

2. Slee, R.: A Knife Blade Found in the Brain Years After Its Entrance. Death Resulting from Other Causes, *Med. News* 59:95-96 (July 25) 1891.

3. Delanglade: Penetration of a Large Knife in the Brain Across the Orbit, *Marseille méd.* 38:681-684, 1901.

4. Vallas: Foreign Body in Brain, *Lyon méd.* 98:362-364, 1902.

5. Kennedy, R.: Case Presenting a Sinus Which Traversed the Cranium Completely and Contained Some Portions of a Straw Hat Carried into the Brain by Means of a Spike, *Glasgow M. J.* 63:42-44 (Jan.) 1905.

ried pieces of straw into the brain. No immediate symptoms followed. Three and one-half months later he suffered drowsiness, febrile disturbance, headache, vomiting and the wound was discharging pus. Examination under anesthesia revealed a large sinus traversing the temporosphenoidal lobe of the brain to the opposite side of the skull which was filled with pus and short pieces of straw. The sinus was cleared out, packed with iodoform gauze, and drained. Complete recovery took place two months later. Examination two years and four months after operation showed the patient to be in excellent physical and mental health.

Gallemaerts:⁶ A girl, aged 5 years, fell while running with a crayon in her hand; the pencil penetrated the left internal canthus 3 cm. into the frontal lobe; it

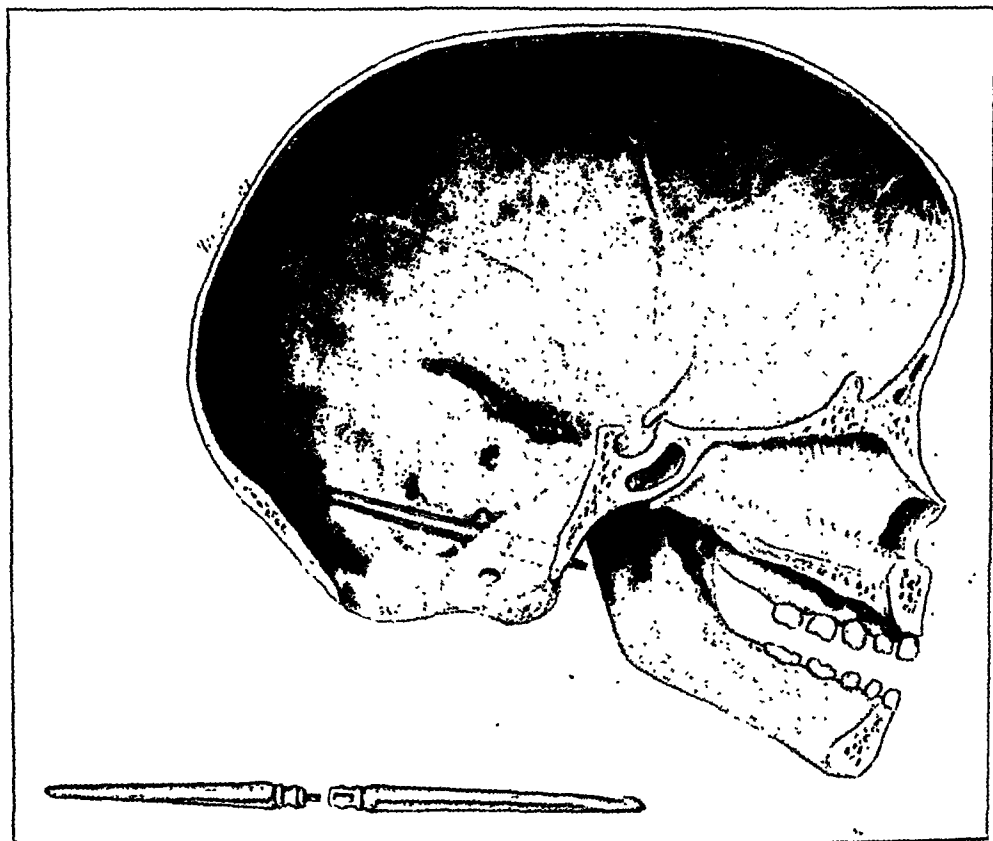


Fig. 4.—Probable position taken by instrument in left jugular foramen and cerebellar fossa.

remained there twenty-four hours before it was extracted with a forceps. Infection followed. Deep drainage was instituted and there was complete recovery after two months. No cerebral or ocular symptoms were noted. One year later the patient died apparently from influenza. Necropsy showed complete softening of the frontal lobe due to a streptococcic abscess extending from in front of the lenticular nucleus to a region of the third ventricle. An abscess had developed gradually, provoking no cerebral trouble but causing pupillary stasis.

6. Gallemaerts, E.: Foreign Body in Brain (Colored Crayon) Penetrating Through the Orbit. *Presse oto-laryngol. belge* 10:529-535, 1911.

Blaine:⁷ A Slav, aged 43, fell from a wagon, striking his head on the pavement; he had headache and vertigo. Roentgen-ray examination revealed a knife blade 1.5 cm. wide and 8 cm. long extending from the right frontal bone to the middle and posterior ethmoid region. Left sided body retardation suggested that the blade had been embedded for the last twenty years; the real cause of the injury could not be learned. A lumbar puncture was made; the Wassermann reaction and the spinal fluid were negative. The patient was discharged after a few days in normal condition.

Gessner:⁸ A chauffeur, aged 34, had a hemorrhage from the left ear and received a diagnosis of probable fracture of the base of the skull. Nine days later he had complete left hemiplegia and was in a sluggish mental condition; the eye grounds were normal. Roentgen-ray examination showed a 2 inch (5 cm.) knife blade stuck through the vertex on the right near the anterior superior angle

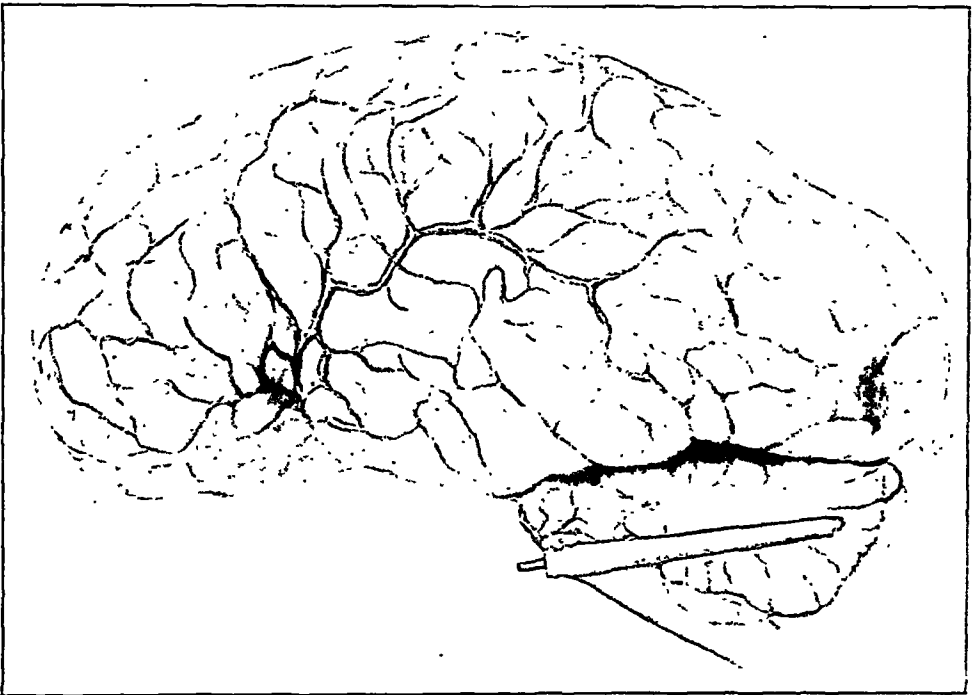


Fig. 5.—Probable position of instrument in left cerebellar hemisphere.

of the parietal bone. An operation for removal of the knife blade was performed on the eleventh day, and one half ounce (15 c.c.) of pus was drained from the track. A cigaret drain was established, with iodoform gauze and bone wax packing. The drain was removed on the thirteenth day, and there was complete and uninterrupted recovery.

McLean:⁹ A girl, aged 5 years, was kicked in the head by a horse; the depressed fracture resulting was operated on at once. A stormy convalescence

7. Blaine, E.: Knife Blade in Brain; Roengen-Ray and Clinical Findings, *Am. J. Roentgenol.* 4:622-624.

8. Gessner, H. B.: Removal of a Foreign Body from Brain. *New Orleans M. & S. J.* 69:636-638 (March) 1917.

9. McLean, S. H.: A Piece of Steel in the Brain Eighteen Years, *South. M. J.* 11:245 (March) 1918.

was followed by recovery six weeks later. At the age of 23, the patient had headaches and twitching of the foot and of the leg. In October, 1915, at operation, a forceps blade $2\frac{1}{2}$ inches (6.27 cm.) long was found between the dura and the skull and was removed. Complete recovery followed one week later, and she was enjoying perfect health two years after the operation. The steel object had been in the brain for eighteen years.

Reynes:¹⁰ A man, aged 25, who was insane, in an attempt to commit suicide tore two picture nails $3\frac{1}{2}$ cm. long from the wall and with a stone drove both nails into the top of his head. No fever, hemorrhage or meningeal symptoms resulted. Some days later, when he confessed the suicidal attempt, physical examination revealed two small scars in the median line of the scalp. Roentgen-ray examination showed two nails embedded in the brain; these were successfully removed with a forceps. A few days later the patient drove a needle into the brain through one of the wounds. Slight symptoms followed. The needle was successfully removed. He died some years later from an unknown cause.

Davison:¹¹ The patient had engaged in a fight and had been stabbed in the left side of the head with a pocket knife, after which he was unconscious for two hours. He slept well that night, was up early the next morning and walked two miles to his own home, where he ate heartily and had no symptoms except from the slight scalp injury; three days later he "turned sick and blind," and though he could still walk he went to bed. On the seventh day the patient noticed a tingling in the foot, leg and hand on the right side. Numbness and finally paralysis developed. He lost control of his bladder and rectum. He did not remember events during the third week, and had only a hazy recollection of being taken to the hospital. There was then complete hemiplegia of the right side. The patient was in a semicomatose condition, although he could be aroused. Roentgen-ray examination showed a knife blade $1\frac{3}{8}$ inches (2.8 cm.) in length in the skull, in the left rolandic area. The author trephined, removing a section of bone 2.5 by 3 cm. with the knife blade in the center. When the section of the skull was lifted, the dura was exposed showing an opening by the blade through which exuded a thick greenish yellow pus. The brain was not pulsating in this area. A crucial incision was made in the dura which exposed an abscess the size of a hen's egg. Recovery followed.

Flesch:¹² A woman, aged 34, was shot twice with a revolver of 7.5 mm. caliber; one of the bullets entered the skull and was localized roentgenologically in the left hemisphere. A paralysis of the left upper and lower extremities soon disappeared. Ten weeks after discharge from the hospital the woman complained of left occipital headache. Roentgen-ray examination disclosed that the bullet now lay in the left occiput. The migration could hardly have resulted through abscess formation or gravity. It was assumed that this might have taken place by way of the lateral ventricle, and experiments on cadavers made this theory seem plausible. At operation, two years later, the bullet was actually found in the left lateral ventricle. Recovery was made.

The literature of cerebellar injury was considerably enriched during the war; some of the papers of this period are mentioned here.

10. Reynes, H.: A Strange Attempt at Suicide; a Degenerate Hammers Two Nails into His Brain with a Stone, *Bull. Acad. de méd.* **84**:102-103 (Oct. 5) 1920.

11. Davison, T. C.: Knife Blade in Brain, *J. M. A. Georgia*, **11**:267 (July) 1922.

12. Flesch: Migration of a Projectile into the Lateral Ventricle Confirmed by Operation, *Arch. f. klin. Chir.* **121**:56 (Dec. 14) 1922.

Milligan¹³ reported in 1916 a case of a soldier wounded at Ypres by a piece of shell which, passing through the skull, had entered the anterior portion of the left cerebellar lobe. Severe hemorrhage resulted,



Fig. 6.—Anatomic structures entering or leaving jugular foramen: *A*, glosso-pharyngeal, pneumogastric and spinal accessory nerves; *B*, meningeal branches from ascending pharyngeal and occipital arteries.

possibly from the lateral sinus. When seen a suppurating sinus led down to the foreign body. Removal was easily effected and complete recovery ensued.

13. Milligan, W.: Removal of a Piece of Shell from the Cerebellum of a Soldier Wounded at Ypres, Proc. Roy. Soc. Med., London, Otol. Sect. 9:31, 1915-1916.

In an article on gunshot injuries of the cerebellum published in 1917, Holmes¹⁴ states that the cerebellum may be regarded as a "motor reinforcing organ." "It seems probable that it takes no direct part in the processes that produce motor effects, whether initiated reflexly or voluntarily, and that it does not augment these, but that it tunes or regulates the activity of certain motor mechanisms, most probably spinal, so that the response to a volitional stimulus is immediate, effective and proportional to the intensity of the cerebral impulse. Astasia is not such a prominent symptom in most local lesions of the cerebellum in man as in animals after experimental destruction, though it varies in degree in different cases. Clinical observations confirm Luciani's conclusions that atonia, asthenia and astasia, the triad of symptoms to which he attributes all the function disturbances, result from cerebellar lesions."

Holmes found with the cerebellum cases under his observation that in many instances the primary wounds were large and the softenings, hemorrhages and septic processes that so frequently accompany such injuries undoubtedly increased the extent of the destruction. The majority of wounds involved the posterior inferior surface of the cerebellum; most of them were referred to the lobus gracilis, but practically every region except the anterior superior portion was affected in one or more cases.

In two patients fragments of bone were driven along the under surface of the tentorium, so that the injury was limited to the superior surface. In others missiles had entered through the occipital or parietal lobes and had penetrated the tentorium. Thus far Holmes has found no definite evidence of localization in the cerebellum. Holmes' findings do not agree with Bárány's views as to functional localization. He says, however, that there can be no doubt that the relative prominence of different symptoms, such as tremor, slowness and incoordination of movement, as well as nystagmus, varies with the site of the lesion.

Holmes in another article cites the case of a man who, in an attempt to commit suicide eight years before the article was written, shot himself through the mouth and produced extensive destruction of one lateral lobe of the cerebellum, in which fragments of metal still remained. Another patient had been wounded by fragments of shell casing twenty months before and had been trephined over the lateral lobe. Details of the results seem to be wanting.

A remarkable case is reported by Jefferson¹⁵ of a Tartar boy, aged 18, a chauffeur who was struck by a bullet 12 cm. above and 1 cm.

14. Holmes, G.: The Symptoms of Acute Cerebellar Injuries Due to Gunshot Injuries, *Brain* 40:461-535, 1917.

15. Jefferson, G.: Removal of Rifle Bullet from Right Lobe of Brain. Illustrating the Spontaneous Movement of a Bullet in the Brain. *Brit. J. Surg.* 5:422, 1918.

behind a line drawn vertically upward from the preauricular point. The bullet track ran downward and backward. Roentgen-ray examination revealed the bullet lying in the right cerebellar fossa. The object lay obliquely, with its nose downward, inward and forward, suggesting that it had been deflected after entering the skull. It apparently was embedded 3 cm. deep in the right lobe of the cerebellum. The chief localizing signs were nystagmus toward the right, a tendency to fall always toward the right, and right sided dysdiadokokinesia. When another roentgenogram was made nineteen days after the injury, the bullet was shown to have sunk backward until it was separated from the inner surface of the occipital bone by barely 1 cm. This general movement backward had been accompanied by version of the bullet, so that its nose which formerly pointed forward, downward and inward, now pointed backward, upward and inward, the general lie of the bullet being now horizontal. The bullet had therefore traversed a distance of 2 cm., its base having gone through a relatively large excursion. The bullet was easily extracted through a trephine opening.

Neuhoff¹⁶ relates some of his war experience in a rather general way. Nothing is said particularly about cerebellar wounds. The total mortality for operated head wounds, including deaths from other causes and deaths after leaving the hospital, was 42 per cent. in dural penetrations in the first series of cases; this was reduced to 29 per cent. in the second series. The author concludes that the ultimate prognosis for patients with craniocerebral wounds after complete early operations is far more favorable and cheering than was generally thought to be the case.

COMMENT

Much has been written regarding traumatic injuries of the brain, especially the cerebrum, and from this literature it is apparent that the individual can survive deep penetrating injuries of this organ even when the object is not removed. Accounts of such injuries involving the cerebellum are extremely rare or, at least, were so until the advent of the medicomilitary literature of the Great War. That penetration of the cerebellum by an object traversing the mouth and entering the skull through a basal foramen is, naturally, most unusual, and careful search of the literature fails to reveal an example. That such an injury can occur and the patient rapidly recover with but slight temporary, and no permanent, disturbances, is shown by the experience of the patient whose history has been described here.

16. Neuhof, H.: The Surgery of Craniocerebral War Wounds and Its Results, Arch. Neurol. & Psychiat. 2:237, 1919.

GROWTH DISTURBANCES FOLLOWING RESECTION OF JOINTS *

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SAN FRANCISCO

The advisability for the resection of a joint in a growing individual with intact, epiphyseal cartilage plates is the subject for as much discussion today as it has been during the last century and a half.

It is of considerable interest to recall briefly the early history of joint resection, bearing in mind the added difficulties in the days before antisepsis and anesthesia. The first resection of the hip joint is accredited to Anthony White in 1721, the first resection of the elbow joint to Wainman in 1758, and the first resection of the knee joint to Filkin about the same time. However, the credit for the first successful resection of the knee joint is generally given to Park of Manchester. His patient, a man aged 33, obtained such a good result that he was able later to go to sea.

Of more direct interest because of its bearing on the subject under investigation is the first successful resection of a knee joint on a young patient, by Syme.¹ This operation performed in 1829 on a boy, aged 8, came out so well that he could walk and run without trouble. It was necessary, however, for him to wear a raise of 2 inches (5 cm.) on the shoe of the operated side. From this time on, we find adherents for and opponents to the resection of joints in growing patients..

Brodie,² in his book written in 1834, says that amputation is the method of choice in infections that do not clear up.

Humphry³ in 1858 made the following statement:

The fact that the growth of a bone in length takes place chiefly through the medium connecting the epiphysis with the shaft has assumed great practical importance since the successful revival of the operation of excision of the knee. It is maintained by some that if the operation be performed in children, the limb will not grow in like proportion with its fellow and therefore will be comparatively useless. This has not been found to be so in all cases, and it is highly probable that the subsequent, proper growth of the limb, will depend in great measure on the quantity of bone that is sawn away. But if care be taken to leave a thin slice of the epiphysis in connection with each of the bones, experi-

* From the surgical laboratory of Stanford University School of Medicine.

1. Syme, James: *Treatise on the Excision of Diseased Joints*, Edinburgh, Southerland and Knox, 1831.

2. Brodie, B. C.: *Disease of the Joints*, London, Longman, Rees, Arme, Brown and Longman, 1834.

3. Humphry, George: *A Treatise on the Human Skeleton*, London, Macmillian Company, 1858, p. 44.

ence has proved it to be pretty certain that the growth will go on with little interruption and a useful limb will be retained.

Humphry has performed several resections in growing persons, and his statements lead one to believe that he had given a great amount of thoughtful consideration to this subject.

Coote ⁴ (1867) says:

I am no strong advocate for the operation of resection of the knee joint under any circumstances, and disapprove of it almost unconditionally in children, in whom the limb afterwards becomes year by year weaker, more withered and less equal to the opposite member.

Koenig ⁵ (1867) reported two successful cases of knee joint resection. One of the patients had a shortening of 1.5 cm., and the other a shortening of 5 cm. He also tabulated 110 other cases by various surgeons, up to that time. He made a study of the variation of the heights of the epiphyseal cartilage from the articular surfaces of both the tibia and the femur at the ages of 11, 16 and 18 years, and gave some useful guides for the protection of the epiphyseal cartilage.

Sayre ⁶ (1876) practiced resection of joints, but in his lectures says:

If the disease is not sufficient to warrant complete exsection, you may remove all dead bone by drilling and gouging; pass setons of oakum or perforated rubber tubing through the joint for drainage, and conduct the treatment on the general plan recommended when speaking of the management of the ankle joint.

Thomas ⁷ (1878) says,

As regards excision of joints, my experience will not allow me to endorse the opinion of Professor Spense, that the operation is "so obviously an advance in the right direction," but I have been convinced that it is a step in the wrong direction. In neglected or wrongly handled cases in some cases there is no alternative and excision is indicated.

In 1892 Whitman ⁸ came to the conclusion from his observation on tuberculosis of the knee joint in children that scientific conservative treatment was preferable to excision of joints. In his recent books he adheres to the same view, and bases his opinion on the facts that there is too great a shortening following complete removal of the epiphysis and that in those cases which might respond to partial excision, cure might be obtained by the conservative method.

4. Coote, Holmes: *On Joint Diseases*, London, Robert Hardwicke, 1867.

5. Koenig: *Beiträge zur Resection des Kniegelenkes*, Arch. f. klin. Chir. 9:177, 1868.

6. Sayre, L. A.: *Lectures on Orthopedic Surgery and Diseases of the Joints*, New York, D. Appleton & Co., 1876, p. 223.

7. Thomas, H. O.: *Disease of the Hip, Knee and Ankle Joints*, London, H. K. Lewis, 1878, p. 168.

8. Whitman, Royal: *Observations on Tuberculous Knee Joint Disease in Childhood*, Arch. Pediat. 9. 1892.

Sherman⁹ (1897) came to the conclusion from his observation on operations on the knees of two children that it is possible to remove the articular cartilages of the femur and tibia and all the ossified portion of the epiphysis, and only interfere to a very limited degree with growth of those bones. He also reported at that time an operation by which he removed the entire ossified part of the epiphysis through a trephine opening over the inner tuberosity of the tibia, and another lesion in the juxta-epiphyseal region of the same bone, which was removed by a similar method.

Townsend¹⁰ (1899) concluded from his own observation that excision of the knee joint should rarely be performed before puberty, but that erosion, arthrectomy and partial operations are to be preferred. Shortening will usually follow and will depend on the amount of bone removed and the age at which the operation is performed. Protection should be given to the knee for a long time after operation to prevent flexion deformity or genu recurvatum. The leg should always be put up straight. In septic cases amputation is to be preferred to excision.

Jones and Lovett,¹¹ in their recent book, state that open operation, except the excision of abscesses, should rarely be called for and never in the early stage of the disease. In acute angular flexion with external rotation and subluxation, it may be necessary in adults to perform wedge excision, removing the joint surfaces and correcting the alignment and displacement. If this is done in young children there is danger of stopping or deviating the growth of the epiphysis and causing serious shortening.

Allison,¹² in a recent article, states that in subjects who have not gained their bone growth, but who have tuberculosis of the knee, it would seem wise to make the diagnosis early by exploratory arthrotomy, to secure the diagnosis by section of tissue removed and by guinea-pig test. In case the disease is positively found to be tuberculosis, the joint cartilage should be removed from the femur, tibia and patella, in order to secure at an early date an ankylosis with the leg in straight vertical position with the thigh, as described by Hibbs for ankylosing the knee joint in adults. He also states that the interference from this operation, in which the integrity of the epiphysis is preserved, is not greater than may occur by the conservative method with the use of crutches, plaster-

9. Sherman, Harry: Erosion of the Knee in Children with Conservation of the Epiphyseal Cartilages, *South. Calif. Pract.* 13:3 (March) 1898.

10. Townsend, W. R.: The Prevention of Deformity After Excision of the Knee in Children, *New York. M. J.* 69:436, 1899.

11. Jones and Lovett: *Orthopedic Surgery*, New York, William Wood & Co., 1923.

12. Allison, N.: The Surgery of the Knee Joint, *Surg., Gynec & Obst.* 39:4 (Oct.) 1924.

of-Paris splints and braces, and the lack of function of the lower extremity throughout the growing period.

Baldwin at the Shriners' Hospital for Crippled Children, San Francisco, favors the careful resection of tuberculous knee joints in children. It was the work at this hospital that gave the impetus for the present investigation.

From this incomplete review of the literature and the writings of others not enumerated, it is found that the majority of surgeons favor the conservative treatment of joint disease in growing persons. This is especially so in the case of the knee joint, in which the adjoining epiphyses is responsible for the greatest increase in length growth. An exact determination of the disturbance in growth in the human limb following operation is rather difficult. It is necessary to exclude an existing shortening or lengthening. There also is the possibility of error in measurement due to tilting of the pelvis and the adduction or abduction of the limb. In order to get some definite data relative to interference in growth following resection of the knee joints, twelve experiments were performed on young growing rabbits. Only four of the experiments will be reported because the other animals did not survive a sufficient time to allow for any deduction.

METHOD

Under general anesthesia, with aseptic precautions, the knee joint was exposed by a curve incision below the patella. The patella ligament was severed or thrown back with a piece of the tubercle of the tibia, after which the crucial ligaments were severed and the semilunar cartilages removed with their attachments. The articular cartilage, with a thin layer of adjoining bone, was removed from the tibia, the femur and the under surface of the patella. Two shallow grooves were cut in the tibia for the reception of the condyles of the femur, and after their approximation the denuded patella was replaced. The patella tendon was sutured in place, and the wound closed in layers. A plaster dressing was applied, extending from the toes to the groin only, as it was found impractical to use a complete spica. Complete fixation was not necessary as these experiments were not intended primarily to cause an ankylosis.

PROTOCOLS

EXPERIMENT 1.—The knee joint of the right leg of Rabbit 09 was opened and the articular cartilage with a thin layer of bone was removed from both the tibia and fibula. Two grooves were prepared in the tibia for the reception of the condyles of the femur. The two approximated bones were kept in apposition by an X-suture of kangaroo tendon passed through each bone. A plaster-of-Paris dressing was applied from toes to groin. The animal died at the end of thirty-six days. There were no signs of union between the tibia and the femur.

A small osseous bridge extended from the upper surface of the tibia to the femur. The measurements of the bones were:

| | Normal | Operated | Difference |
|------------|---------|----------|------------|
| Femur..... | 5.8 cm. | 5.8 cm. | 0 |
| Tibia..... | 6.5 cm. | 6.1 cm. | 0.4 cm. |

Thus, there had been no disturbance in growth up to this time, as any difference in length could be accounted for by the amount removed at the operation.

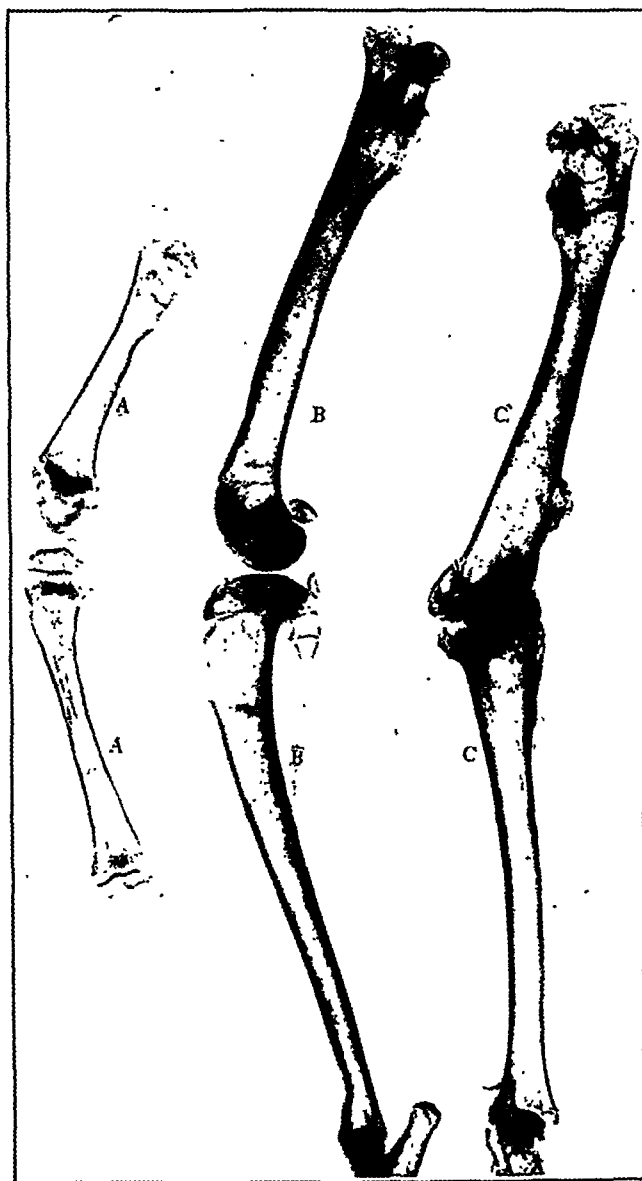


Fig. 1 (Experiment 2).—*A*, relative size of bones at time of operation; *B*, normal bones (comparison should be made of *A* and *B* to get normal amount of growth), and *C*, operated bones showing resected knee joint (comparison should be made with *B* to get idea of growth disturbance; total loss of growth was 1.2 cm.).

EXPERIMENT 2.—The same method was used for Rabbit 02, aged 2½ months, as in Experiment 1. The two approximated bones were held in position by a kangaroo tendon suture, passed through the tibia and femur. The experiment

was terminated at the end of 162 days. There was firm union at the site of resection. When the region of the resection was cut through, one saw an osseous bridge connecting the two bones, although it did not extend along the entire denuded surfaces. Figure 1 shows the condition that existed at the end of the experiment. The measurements of the bones were:

| | Normal | Operated | Difference |
|------------|----------|----------|------------|
| Femur..... | 9.9 cm. | 9.2 cm. | 0.7 cm. |
| Tibia..... | 10.1 cm. | 9.0 cm. | 1.1 cm. |

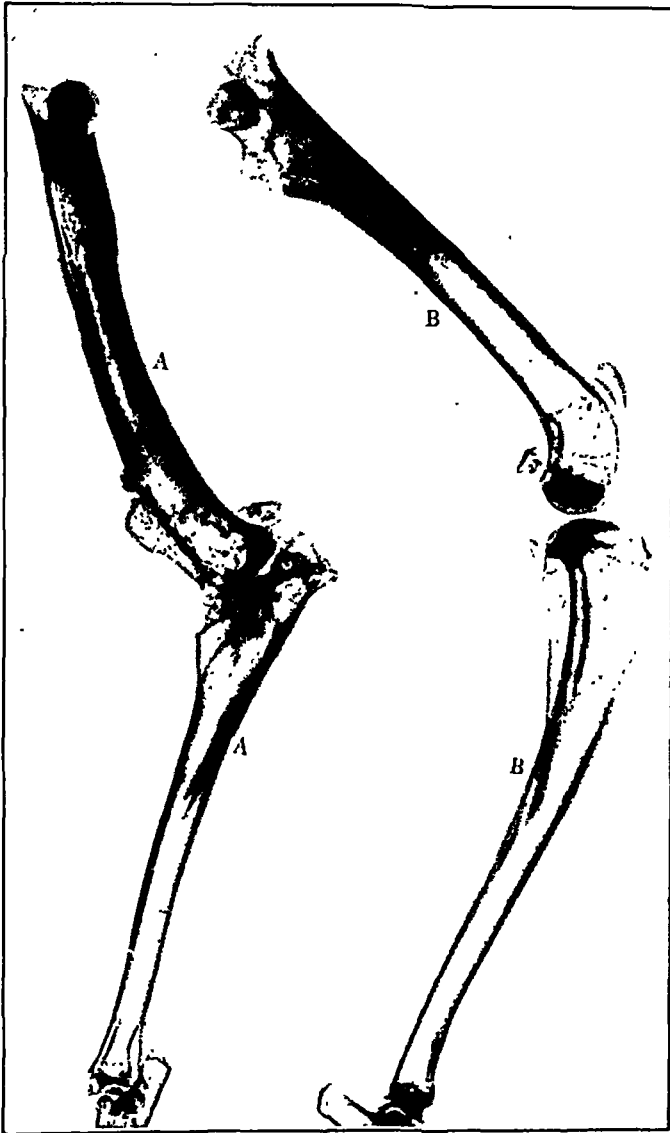


Fig. 2 (Experiment 3).—*A*, operated bones showing the resected joint in recurvation (total loss of growth was 0.4 cm.), and *B*, normal leg for comparison.

There was a total loss of 1.8 cm. on the side of the resected joint, about 0.6 cm. of which could be accounted for by removal of bone at the time of the operation.

Microscopically, the sections through the site of the resection did not show a definite continuity of bone at any one place, although it is possible that a serial

reconstruction would have established that fact. There was a large amount of new bone formed on both the denuded bones.

EXPERIMENT 3.—The same operation was performed on Rabbit 07 as in Experiment 2.

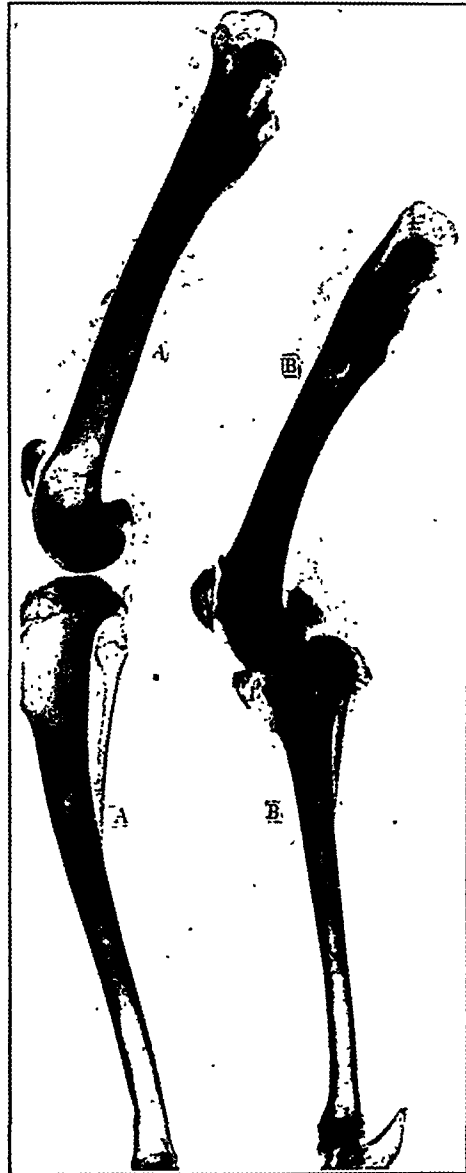


Fig. 3.—*A*, normal bones, and *B*, operated limb with resected joint; loss of growth was 2.7 cm. Greater loss in growth was possibly due to sutures injuring the epiphyseal cartilage plate.

At the end of 222 days, there was a slight amount of motion in the resected joints. Figure 2 shows a considerable amount of new bone and it is difficult to determine whether union had taken place. The measurements of the bone were:

| | Normal | Operated | Difference |
|------------|--------|----------|------------|
| Femur..... | 8.5 | 7.9 | 0.6 |
| Tibia..... | 9.4 | 9.0 | 0.4 |

Allowing for the bone that was removed at operation, there was little loss in growth due to the operation.

Microscopically, there was a large amount of new bone about the resected surfaces, although there was not a complete bony bridge connecting the two bones.

EXPERIMENT 4.—The operative procedure described in Experiment 1 was used on Rabbit 03, aged 2½ months, except that the kangaroo suture extended through the metaphysis of the tibia.

At the end of 261 days, a slight amount of posterior luxation of the tibia on the femur took place. The resected joint was stable to lateral stress but there was some anteroposterior play. A bony bridge connected the tibia and the femur at one place. Figure 2 shows the relative size of the operated and the normal bone. There appeared to be an osseous bridge connecting the two bones. There had been a retardation in growth of the two bones; of the tibia more than the femur. The measurements were:

| | Normal | Operated | Difference |
|------------|--------|----------|------------|
| Femur..... | 9.3 | 7.3 | 2.0 |
| Tibia..... | 10.2 | 8.7 | 1.5 |

If we allow 0.8 for the width of the bone and cartilage removed at operation, there still remained 2.7 cm. shortening. The total normal growth during the period was 8 cm., so there had been a retardation of about one fourth of the actual growth during the experimental period. The large amount of growth loss following this resection might have been due to the fact that the restraining suture passed through the metaphysis causing further disturbance to the actively growing cartilage cells of the epiphyseal cartilage plate. In none of the other experiments was there a loss in growth of more than 1.2 cm., which is relatively slight when it is considered that the average growth during this period was about 7 cm.

CONCLUSIONS

1. A careful resection of the knee joint, in which the entire articular cartilage and a thin layer of adjoining bone is removed, will cause practically no disturbance in length growth.

2. It is important not to injure the epiphyseal cartilage plate and to refrain from passing fixation sutures through the actively growing columns of cartilage cells.

3. It is advisable not to strip up the soft parts too near to the epiphyseal cartilage plate because of the chances of injuring its blood supply and thereby causing some growth cessation.

4. All measurements in these experiments were controlled by measuring the roentgenograms taken at a uniform target film distance. This is considered as being the most accurate means of measuring the length of bones on the living subject.

PRIMARY CONGENITAL MEGALO-URETERS *

J. S. EISENSTAEDT, M.D.

CHICAGO

Primary congenital megal-ureter is the occurrence of enormous bilateral caliber of the ureter in cases in which there is no demonstrable obstruction to the urinary outflow as determined at necropsy or by complete examination during life. The condition has been observed in the fetus, in the new-born and in early life.

Similar cases to those reported here appear in the literature under the title of congenital dilatation of the ureters. The term dilatation is ill chosen because the so-called dilated ureters of the type to be described here probably never were of normal caliber and may represent the persistence of a stage in early fetal development. The expression dilatation of the ureters should be reserved for those cases in which there is definite pathologic condition or anomaly that accounts for the widening of the ureteral lumen. These cases may be congenital or acquired. In fact, the condition may exist in early intra-uterine life, but the cause, usually an obstruction, is determinable by thorough examination.

Several of the cases reported have been in association with and secondary to obstruction in the urethra or at the vesicle end of the ureter. Several instances were due to hypertrophy of the verumontanum. Many cases of acquired dilatation of the ureter are, of course, secondary to calculus, tuberculosis and chronic pyelocystitis. This article, however, does not concern cases having a definite or demonstrable etiologic factor.

Attention may first be called to the disturbance when complicating pathologic conditions produce subjective symptoms. No etiologic factor is determinable and the lesion may occur with other congenital defects. Complete reflux of fluid from the bladder to the renal pelvis is present in full column.

CASES IN THE LITERATURE

At the seventeenth congress of the French Urological Society, Papin and Legueu¹ reported four cases of enormous dilatation of both ureters. The ureters were widely dilated from end to end and had large gaping orifices. There was no demonstrable obstruction to the urinary outflow. All four cases showed:

1. Great dilatation of both ureteric orifices, which were gaping and showed no movement of opening and closing.
2. Complete communication between the bladder and the renal pelvis.

* From the urologic service of the Michael Reese Hospital.

1. Papin: Chapter on Anomalies, *Encyclopédie Française d'urologie*, 1914.
Papin and Legueu: *Arch. urol. de la Clin. de Necker* 1, No. 4.

3. Complete filling of the urinary tree when the bladder is filled with collargol, as demonstrated by roentgenogram.

At the last meeting of the French Urological Association before the war, Hallé reported a necropsy on a girl, aged 5 years, with marked dilatation of both ureters and with no demonstrable obstruction anywhere in the urinary tract.

Couvelaire² reported a case of dystocia in a female fetus with a normal urethra but in which there was enormous dilatation of both ureters. John Thompson, in discussion of this case, suggested a disturbed nervous mechanism.

Saintu³ reported a case of dystocia at 7½ months. The fetus had enormously dilated ureters, which at the narrowest portion measured from 6 to 8 mm. in diameter. There was no urethral obstruction.

Ahlfeld presented a case of a fetus with marked dilatation of the ureters and bladder without the presence of any obstruction.

Longridge⁴ briefly reported two stillbirths, both girls, with no urethral obstruction but with enormous dilatation of both ureters.

At the last congress of the German Urological Association, Kielleuthner⁵ reported five cases of congenital dilatation of the ureters. His report thus far has appeared only in abstract and his conclusions as to the mechanism in these cases are not stated.

Hyman⁶ reported the case of a 7 year old boy with moderate hypertrophy of the bladder and enormous dilatation of both ureters. The etiology of the condition was not determined. The ureteric orifices were patulous and demonstrated complete reflux to both pelvis.

Delmas, in his work on anomalies of the ureter, simply states that congenital dilatation of the ureters has been seen.

Corsy,⁷ Ballantyne,⁸ Böstroen,⁹ Morris, Hyman⁶ and others have reported cases of congenital dilatation of the ureter in the fetus and in early life associated with obstructive anomalies of the lower urinary tract. It is noteworthy that the available literature on the subject is scant and practically presents no discussion of the pathogenesis or mechanism of this rare pathologic entity.

EMBRYOLOGIC CONSIDERATIONS

The ureteral bud appears on the dorsal side of the wolffian duct in the beginning as a rather wide body. It narrows down to a uniform

2. Couvelaire: *Bull. Soc. anat. de Paris* 2:287, 1909.

3. Saintu: *J. de méd. de Paris* 8:332, 1896.

4. Longridge: *Tr. Obst. Soc., London*, 49:215, 1907.

5. Kielleuthner: Discussion and demonstration in *Ztschr. f. urol. Chir.* 16:236, 1924.

6. Hyman, A.: *Internat. J. Surg.* 35:126, 1922.

7. Corsy, F.: *J. d'Urol.*, 1921, p. 185.

8. Ballantyne: *Antenatal Pathology*, 1902.

9. Böstroen: *Beit zur pathologischen Anatomie der Nieren*, Freiburg, 1884.

caliber by the end of the second month, at which time it is without musculature. Muscle fibers appear next to the bladder at the beginning of the third month and gradually extend upward until they are present at the level of the renal pelvis, about the middle of the fourth month.



Fig. 1 (case 2).—Urinary tract filled with sodium iodide solution; enormous size of bladder and both ureters, with complete reflux to both renal pelves, should be noted.

Gerard,¹⁰ working under Papin's direction, found that the ureter in fetuses up to the fourth or fifth month is of enormous caliber as compared with the kidney and the rest of the body. He states that it can readily be supposed that the organ instead of diminishing in caliber from

10. Gerard: These de Paris.

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this period, as is normal, can continue to develop concurrently with the rest of the body and remain, even in adult life, as voluminous in caliber as it is in early fetal life.

Lorain,¹¹ in his thesis on dilatation of the ureter, states that this type of ureteral dilatation may represent the norm in "the first stage of embryonal life (*Au premier stade de la vie embryonnaire*)," and that it is not surprising that a certain number of dilatations of the ureter should be of congenital origin, because the urinary system affords not uncommonly many abnormalities, from a mild hypospadias to those that are incompatible with life itself.

I have found a wide caliber of the ureter in the earliest weeks of fetal life but no uniformity of this characteristic after the tenth or eleventh week. Some of the ureters examined at this stage have been wider than others. This observation has also been noted by Kampmeier¹² in the pelves and calices in a few early fetal kidneys which he examined while doing his excellent work on "Origin of Congenital Renal Cysts." The subject considered here was not of interest to him at the time of his research and he does not have any statistical data as to the frequency of the wide pelvis and major calices.

REPORT OF CASES

History.—The two cases of primary congenital megaloureters which I have observed both occurred in little girls. Patient 1 was 5 years old when first observed; patient 2 was 7½. Both entered the service of Dr. I. A. Abt at the Sarah Morris Hospital for Children. Because of the practically identical nature of the histories, symptoms and conditions observed, I shall report the cases together.

Both girls entered the hospital with the history of dysuria and increased frequency of urination since earliest childhood. The urines of both were turbid and contained many leukocytes and bacteria. Colon bacilli and staphylococci were present in the urines, the former predominating. The general condition of the younger child, patient 1, was obviously poorer than that of the elder. The temperature variations were greater in the younger child. At the time of the first examination both were able to make daily use of the playroom.

The younger child died and we have a complete report of the necropsy findings of the intra-abdominal viscera. The elder child is alive and to date in excellent condition except for the pathologic condition of the urinary tract.

The general physical examination was negative except that the younger child had a prominent abdomen. This had been noted intermittently since her third year.

Cystoscopic Examination.—Cystoscopic examinations also were practically identical. There was no obstruction or pain on the passage of the cystoscope. There was no obstruction in the urethra as determined by olive tipped bougies. The bladder contents were moderately turbid, the bladder tolerance good or increased. Both children required repeated washings of the bladder to obtain a medium clear enough for accurate observation.

11. Lorain, A.: Thèse de Paris 30, 1921.

12. Kampmeier: Personal communication to the author.

A slight to moderate grade of cystitis with indistinct vascular markings, especially in and about the trigonum, was found in each case. Practically the entire mucosae were involved to lesser degree. A moderate degree of trabeculization was noted, of mixed type rather than of the distinctly coarse variety. At the usual location of the ureteric orifices huge openings were seen symmetrically placed; in the first instance these were thought to be the openings of diverticula. They proved, however, to be the very wide gaping, rigid ureteric orifices. They averaged from at least 1.5 to 1.6 cm. in diameter and did not contract or show the slightest movement on repeated examination. The internal urethral orifices were negative.

Cystograms taken to demonstrate the size and location of the suspected diverticula revealed some enlargement of the bladder and a complete filling of the urinary tree to the pelvis of both kidneys. There was no demarcation between bladder content and ureteric content and the ureters were seen to be

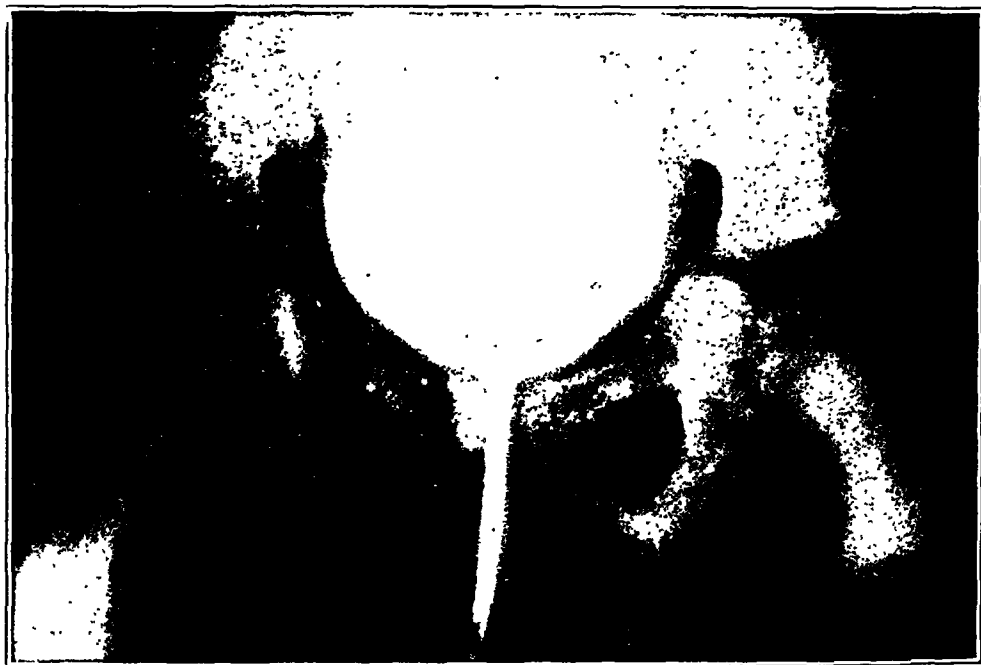


Fig. 2 (case 1).—Enormous bladder.

many times their normal diameter and apparently much too long for the torsos of the children. The hips of the children were not elevated when roentgenograms were made.

Postmortem Examination.—The postmortem examination¹³ of patient 1 by Dr. David B. Witt yielded the following anatomic diagnosis: bilateral dilatation of the ureters; bilateral pyonephrosis; hypertrophy of the bladder; chronic interstitial nephritis and acute splenitis.

The kidneys, ureters and bladder were removed together. The right kidney measured 7.8 by 4.5 by 2.7 cm.; the left 8. by 4.5 by 2.2 cm. The capsule of each was adherent and removed with difficulty. The ureters were greatly dilated, the right more than the left. The latter was 0.9 cm. in diameter at its midportion and

13. In this report the word dilatation is the pathologist's, and while it is in common use referring to this condition, is a misused term in this connection.

1.2 cm. in diameter in its lower third. The right ureter was 1.5 cm. in its upper third, 1.9 cm. in its middle third, and 0.9 cm. in its lower third. On section of the kidneys and ureters, the pelves and calices were found to be greatly dilated and filled with cloudy, purulent fluid. The medulla of each kidney had largely disappeared through the dilatation, the calices being covered by a layer of kidney tissue averaging 1 cm. in thickness. The ureters also were filled with purulent

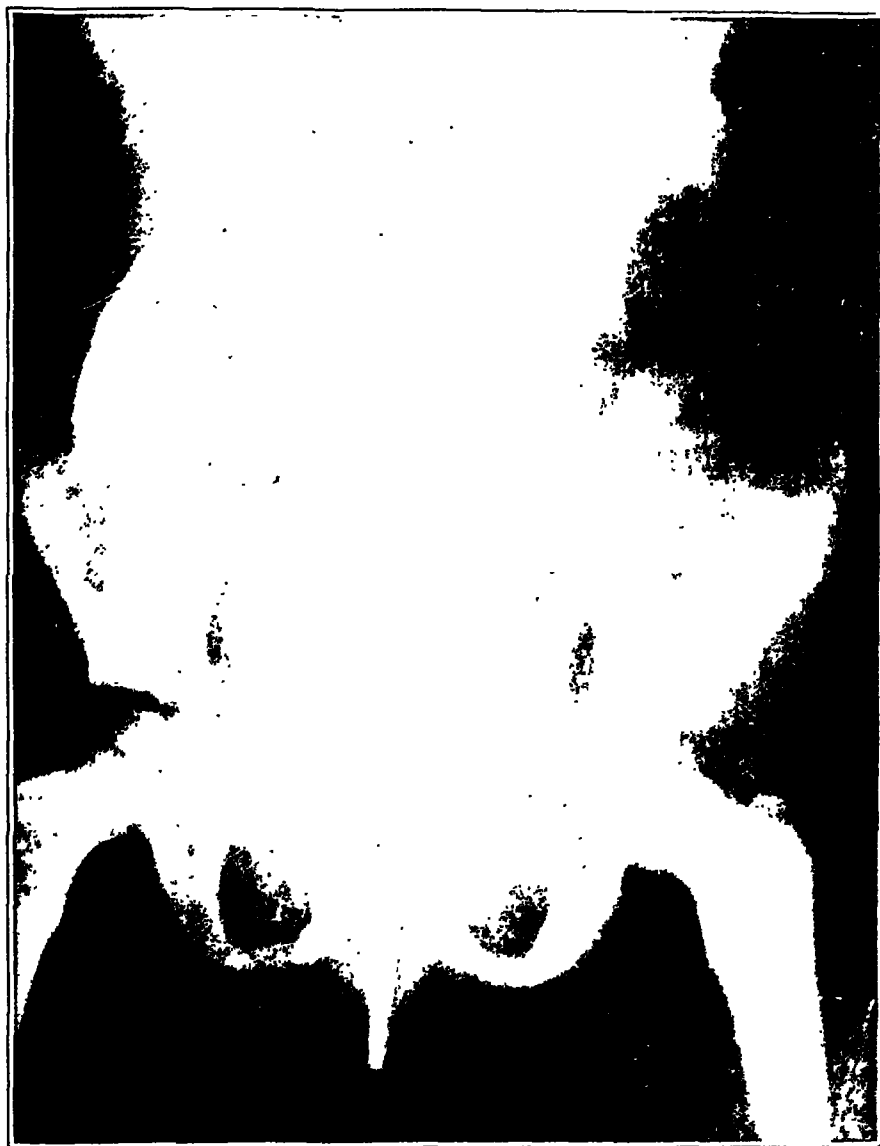


Fig. 3 (Koll's case).—Bilateral megaloureters with two ureters on right side.

fluid. Their inner surface was pale and smooth. At the ureteropelvic junction of each kidney were several horizontal folds, but these did not encroach on the lumen sufficiently to offer hindrance to the flow of urine. Two centimeters below this region the wall of the right ureter contained a hard, almost cartilaginous area which was poorly defined. At their lower ends the ureters opened into the bladder by wide mouths which offered no obstruction. The bladder was contracted and contained a small amount of cloudy fluid. It measured 7 by 5 by 4 cm.

the wall was from 0.5 to 1 cm. thick. The inner surface was trabeculated and had a number of small hyperemic areas. The urethra was patent and offered no obstruction to the passage of a large probe. From the gross examination the dilatation of the ureters, the pelves and the calices appeared to be secondary to the condition that had led to the hypertrophy and trabeculation of the bladder. However, no mechanical obstruction to the outflow from the bladder could be seen.

Microscopically, the pelvic epithelium was found to be absent in areas of considerable extent. The surface of such areas was covered by a mass of leukocytes. A rather broad zone of medullary tissue next to the surface was cellular; it contained lymphocytes, leukocytes and fibroblasts, the tubules being widely separated in this tissue. The medulla was diffusely fibrous; scattered throughout the fibrous tissue were moderate numbers of lymphocytes, plasma cells and eosinophils. The medulla contained only a few tubules of normal size; these were filled with pus cells. Minute, almost completely atrophied tubules were numerous. In the cortex there had also been widespread replacement and atrophy of the tubules by cellular stroma that was infiltrated by round cells. Tubules of nearly normal size were few in number and occurred in widely separated groups; their epithelium was low and their lumens were filled with leukocytes. A few glomeruli had been atrophied, but on the whole the slight involvement of the glomeruli, as compared with the tubules, was striking. The tufts appeared normal in such glomeruli; the capsule was slightly thickened by the surrounding interstitial fibrosis. In one area some of the glomeruli were granular and necrotic and the tubules distended by granular material. Scattered about in the proliferated interstitial tissue were islands of dense lymphoid infiltration. The striking feature of the kidney was the disappearance of secreting tubular parenchyma within the cortex.

The wall of the left ureter was moderately thickened and in general densely fibrous. Surface epithelium was absent. A thin inner zone was cellular, being densely infiltrated by lymphocytes, intermingled with which were a few fibroblasts. Narrow bands and larger islands of lymphoid infiltration separated some of the bands of the deeper tissue. Several islands of dense lymphoid infiltration were present in the periureteral fat. In the right ureter the increase in thickness of the wall was due to the formation of a thick layer of dense fibrous tissue outside the outer muscle coat. Muscle tissue was not increased, but rather partly atrophied; its bundles were separated by bands of round cell infiltration.

The lining epithelium of the bladder was absent except in a few cryptlike folds that dip down for a slight distance into the tissue. A thin superficial zone was richly infiltrated by lymphocytes and plasma cells and contained a few leukocytes and eosinophils. The wall contained smooth muscle, the muscle increase involving both the inner and the outer coats. Just beneath the cellular inner zone were numerous small calcium masses.

As revealed in the accompanying illustrations the bladders were rather large and well filled; the ureters were enormously and about equally dilated. The ureters were apparently too long for the torso and sausage-like segments were apparent. Furthermore, at no place in the entire ureter did its diameter even approach the normal caliber. The renal pelves and calices were also seen to be markedly dilated. There was absolutely no evidence of any organic obstruction on examination nor was any found in the child examined postmortem. Whether or not an obstruction existed in fetal life not determinable at the time of examination or necropsy is another question. Torsions or folds in the ureter are noted, however, in about 20 per cent of new-born children.

The chief characteristics of the cystogram of primary congenital megalo-ureter which differentiate it from the acquired type and the congenital type due to obstructive processes are:

1. The bladder is enlarged and shows increased capacity.

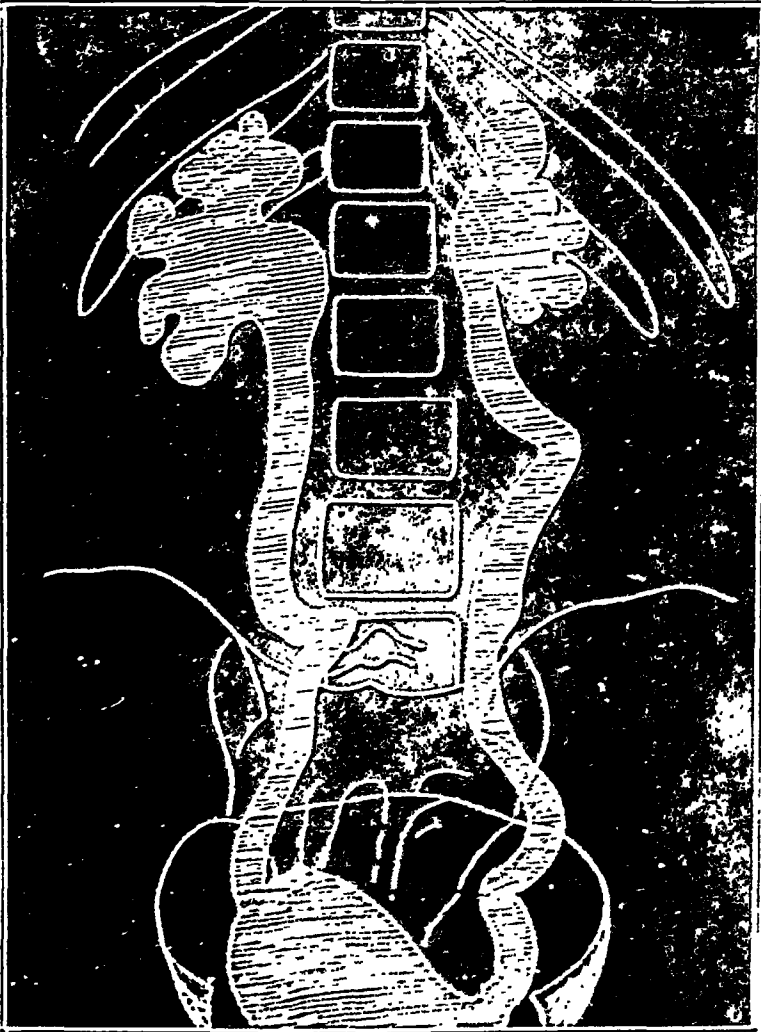


Fig. 4 (Lorain's case).—Drawing made from roentgenogram.

2. There is no evidence of obstruction in any part of the tract due to any mechanical condition, such as stone, valve or stricture of the ureter or urethra.

3. The filling of the ureteral trees is bilateral, complete and symmetrical and practically equal on both sides, and reflux is complete without any pressure other than that of the filled bladder.

4. There is no demonstrable demarcation between the filling fluid in the bladder and that in the ureters.

I have seen a number of dilatations of the ureter resulting from such well understood etiologic conditions as stone, tuberculosis, prolonged pyelocystitis and various lesions of the spinal cord; no case studied, however, has presented all the characteristics that have been enumerated.

THEORETICAL CONSIDERATIONS

In the absence of any determinable obstructive cause the mechanism of congenital megalo-ureters may involve:

1. Deficient development in the musculature of the ureter. The musculature of the ureter does not begin to develop until the beginning of the third month and does not reach the renal pelvis until the middle



Fig. 5 (Legueu and Papin's case).—Appearance of ureteric orifices.

of the fourth month. The possibility of an imperfect development of the muscle fibers, a true hypoplasia, must be seriously considered. This likelihood plus the persistence of the wide caliber of the ureters, as in early fetal life, might explain the mechanism of the condition.

2. An inhibitory influence on the growth of the ureter, as Girard suggests, should manifest itself during the fifth and the sixth intra-uterine month. This may not exert its influence and the ureter continue to grow in length and caliber at a time when it should cease to do so. Were this the cause, however, one would expect the tissues of the enlarged ureters to be normal as observed microscopically.

3. The ureter, like the renal pelvis and the major calices, as noted by Kampmeier, may be very wide in certain fetuses. This is merely another way of saying that no cause can be found in certain cases.

4. In early intra-uterine life some obstruction may exist, probably at the bladder outlet, which is later not demonstrable.

5. A disturbed or deficient nervous mechanism, as Thompson suggested in discussing Couvelaire's case, may be at fault. This point of view cannot be disregarded, because the resemblance of the ureteric

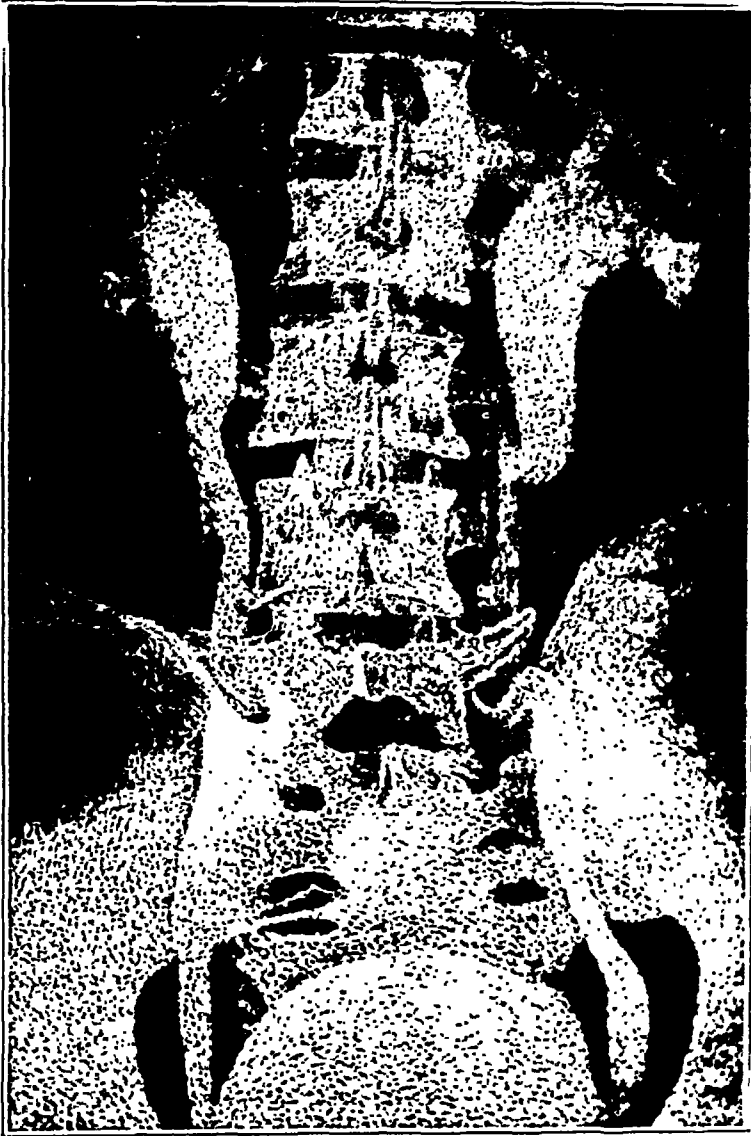


Fig. 6 (Gaudino's " case).—Drawing made from roentgenogram.

orifices to those seen in patients suffering from certain cord lesions was striking and the reflux of fluids from the bladder to the renal pelvis was similar. The trabeculation noted in the bladders of both children likewise simulated, though not perfectly, the type seen in some patients

suffering from cord lesions. And this I interpret as a labor hypertrophy due to the shortening of the intervals of bladder contraction. I have never seen any patient with spinal cord disease show such bilaterally wide orifices and such excessive caliber of the ureters. The spinal cord of the child who died, unfortunately, we were not permitted to remove for examination, but during life she showed no evidence whatsoever of a cord lesion. Patient 2, still living, likewise does not show any symptoms referable to the nervous system.

The necropsy findings of inflammatory round cell infiltration and atrophy of the muscle fibers might suggest that the large caliber of the ureters and the huge rigid orifices were secondary to a long continued inflammatory process, but the presence of identical findings in the fetus and in still-born children would lead one to believe that the wide caliber of the ureters and their huge orifices were primary conditions and not due to an inflammatory process.

SUMMARY

1. Congenital bilateral megalo-ureter may occur without demonstrable cause and, hence, is called primary.
2. The cysto-ureterograms and cystoscopic findings are characteristic, as observed in the two cases reported here.
3. The mechanism underlying the development of this condition may be explained by embrologic considerations, probably a deficiency in the development of the musculature of the ureters.

SARCOMA OF THE STOMACH*

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Sarcoma as opposed to carcinoma ranks low in the tumors of the gastric wall. Various percentages are given in the different clinics; it remains well under 5 per cent of the malignant conditions. Just why this is so is hard to understand unless we take into consideration the great amount of epithelial surface exposed to constant chemical and mechanical assault. The connective tissue elements are much less in relative amount and are little exposed to injury of any sort. In this respect the relative frequency of sarcoma and carcinoma of the stomach is comparable to the corresponding tumors of the uterus.

As to the etiology of sarcoma, here as elsewhere nothing is known; the point of origin is usually the musculature but may be any of the connective tissue elements of the organ. The diagnosis is rarely made. At most a tentative diagnosis of malignant tumor can be entertained. The outstanding feature of a large number of cases is the symptomless development up to a certain stage, followed by rather pronounced symptoms suggestive of ulcer, even of perforation.

The treatment of sarcoma of the stomach is as yet purely surgical, consisting of wide resection, pylorectomy, and, rarely, a palliative gastro-enterostomy.

The literature of this rather rare affection has been thoroughly worked up by the Mayos and more especially by Dr. John Douglas.

The following two cases seem worthy of report because the disease is still a rare one and because two widely different types of sarcoma are present—one closely resembling the typical calloused ulcer, or early carcinoma, the other being more like a mild acute pancreatitis—and because both patients recovered from operation. Curiously enough, the patient with the more malignant type is still well and without symptoms nearly three years after operation, while the other, with an apparently milder type, suffered a recurrence and died within two years.

REPORT OF CASES

CASE 1.—A man, aged 34, born in the United States, entered the New York Hospital, April 26, 1920, in the service of Dr. Charles L. Gibson. He weighed 120½ pounds (55.6 Kg.). He was discharged, May 11, weighing 112 pounds (50.8 Kg.). His complaint on entering was pain in the epigastrium. The present condition was that for five or six months he had had pain in the epigastrium one-half to one hour after meals, with gas and sour eructations, gnawing and burning; these were relieved by soda or vomiting and made worse by food. The pain was

* From the first surgical (Cornell) division of the New York Hospital.

rather high and along both costal margins. There was a tender spot just to the right of the midline halfway from the ensiform to the umbilicus. The symptoms were relieved by a meat free light diet, and entirely relieved by a milk diet and soda; they returned at once on resumption of solid food.

Before the onset of symptoms there had been marked constipation for two months, but the bowels had been regular of late. There was a severe vomiting spell two weeks before the patient entered the hospital, followed by a black stool for two days. There was no blood in the vomitus. He had lost 20 pounds (9 Kg.).

The past history was negative as to previous similar attacks. He had had no operations. There was no polyuria, no dysuria, no serious illness of any sort. The family history was negative.

The physical examination showed a fairly well developed and well nourished young adult who did not appear acutely ill. There were no abnormal findings in the head, neck or chest. The abdomen was flat, almost scaphoid, and symmetrical. There was slight tenderness in the umbilical and epigastric regions. No mass could be felt; the extremities were negative. The liver, spleen and kidneys were not felt.

A provisional diagnosis of gastric ulcer was made. The temperature, pulse and respiration were normal. Gastric analysis of 30 cc. of greenish brown fluid showed a moderate amount of mucus, free hydrochloric acid 68, total 90. The guaiac reaction was positive. Microscopically, there were some red blood cells, mucus and food remnants. A fractional Ewald test was performed, running 20-70 free, 35-90 total at one hour and fifteen minutes. It is interesting that the post-operative fractional Ewald test ran 0-5 for free acid, and 5-21 for total acidity.

A pylorectomy for sarcoma was performed by Dr. Gibson, April 28, under ether; it took one hour and forty-five minutes. The condition was fair; the pulse ran from 80 to 130 at the end of the operation. A high right rectus incision was made; an indurated, irregular mass the size of the palm of the hand was found on the posterior surface of the stomach adjacent to but not impinging on the pylorus. An obviously enlarged lymph node was found just above and another just below. No other metastases were seen or felt. The stomach was not adherent.

Resection of the distal one third of the stomach and closure of both stumps with a Payr clamp and cautery, reinforced by two rows of sutures was the procedure used. Posteriorly, a no loop gastro-enterostomy was performed, using tongue depressor clamps and five rows of suture, three posterior, the first and last silk, the others chromic catgut.

Microscopic examination showed sarcoma of the stomach, which was ulcerated. The specimen consisted of a resected portion of the stomach, the seat of an ulcer 5 cm. in diameter; the edges were overhanging. The ulcer was shallow and had a thick base, measuring 1 cm. The base consisted of a layer of homogeneous soft white tissue, 1 cm. thick. Outside this was a layer of denser connective tissue. Microscopically, the base of the ulcer consisted of a new growth composed of large polyhedral and round cells resembling a sarcoma. It did not infiltrate the muscle coats. The surface was ulcerated. A small lymph node showed no involvement. A later report stated that there was a dense collection of darkly nucleated cells and medium size round cells between the mucosa and the muscular coats of the stomach. This collection was not sharply circumscribed but tended to invade the muscularis mucosae and the muscularis. There were some mitotic figures present and the cells were neoplastic. The mucosa of the stomach was normal. The appearance was that of a lymphosarcoma. This diagnosis was confirmed by Dr. James Ewing.

The postoperative course was uneventful. The usual postoperative treatment of ice cap and rectal drip was instituted, and nothing was given by mouth for twenty-four hours. There was some vomiting up to May 1; this was relieved by lavage. The wound healed by primary union.

The follow-up notes were as follows: November 3, the patient had some gas after food; he had gained 24 pounds (10.9 Kg.). Jan. 9, 1922, he felt absolutely all right; his weight was 133 pounds (60.3 Kg.). Jan. 2, 1923, he felt absolutely all right; his weight was 141 pounds (64 Kg.); he ate everything in limited quantity.



Fig. 1 (Case 1).—Sarcoma of stomach.

CASE 2.—A man, aged 28, Jewish, entered the hospital July 5, 1921, and was discharged August 15. He complained on admission of pain in the epigastrium and difficulty of breathing of twenty-four hours' duration. July 4, in the morning he was taken with a sudden onset of pain in the epigastrium to the left of the midline under the costal margin. He also noticed that it was hard for him to get his breath. He couldn't get the air in. The pain was not sharp and did not radiate. There was no pain in the back, no indigestion and no jaundice. The bowels were constipated. He insisted that up to July 4 he had been in perfect health in every way. His past history was negative. He had never been sick before, and had no digestive disturbances but suffered from habitual constipation.

The family history was irrelevant. He had never had venereal disease nor any nervous symptoms.

Physical examination showed a well developed, well nourished man lying quietly in bed. The head, neck and thorax were negative. The abdomen showed moderate tenderness and rigidity in the upper portion, mainly to the left. The spleen, liver and kidneys were not felt. The extremities and the lymphatics were normal. The urine showed a faint trace of albumin and a few leukocytes. The temperature was 103, pulse 102, respirations 24.

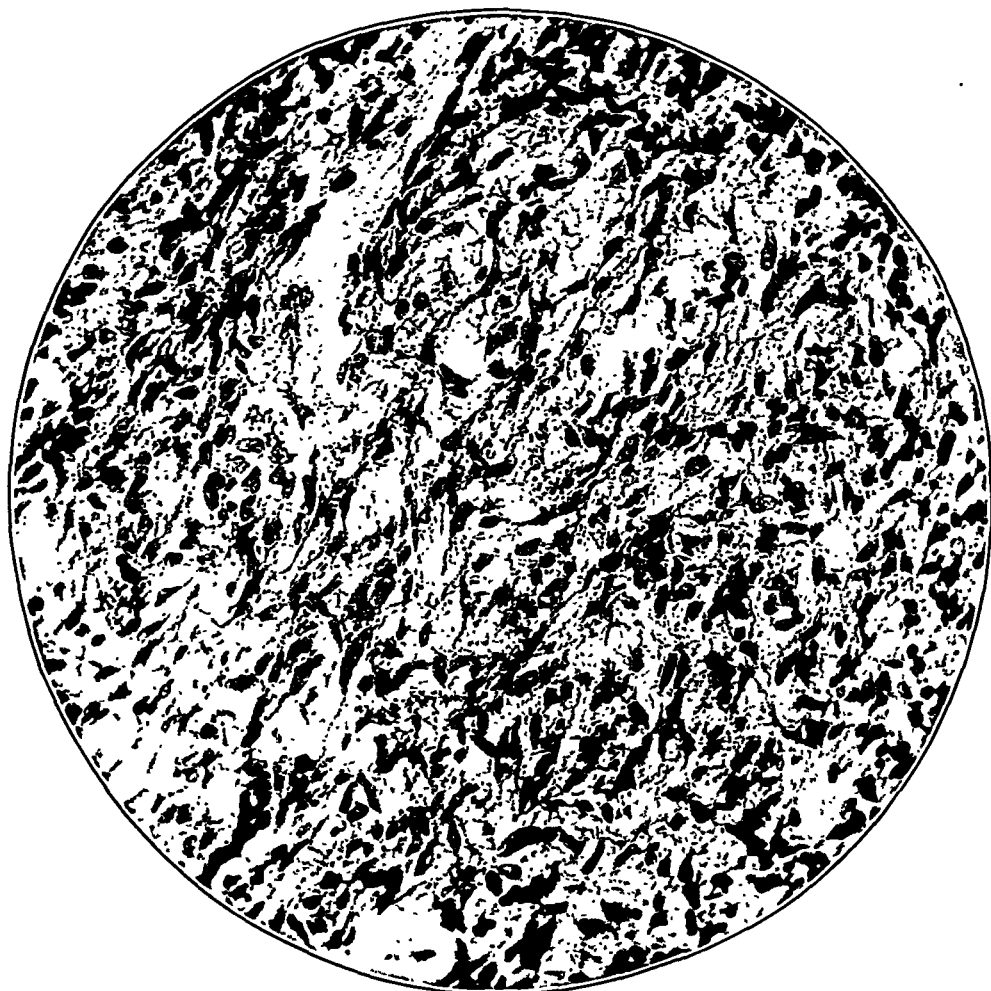


Fig. 2.—Perforating sarcoma of stomach in which resection was done.

The tentative diagnosis by the medical staff was perforating gastric ulcer; by the surgical staff, acute pancreatitis.

July 6, I operated, making a right rectus incision with an additional transverse cut. There was a perforating sarcoma of the stomach 10 cm. in diameter about two thirds of the way to the cardia on the anterior surface near the lesser curvature. It was pedunculated, round, bluish and apparently vascular. It was covered with omentum and there was a slight deposit of fibrin. When the omentum was lifted the mass tore partly loose, leaving a 2 cm. perforation in the stomach wall. There was no bleeding of any moment. The condition was deemed inoperable from the standpoint of radical cure and a wide excision was

done, about two thirds of the anterior wall of the stomach being removed. A plastic suture was then carried out to prevent hour-glass formation, using two layers of chromic catgut. A cigaret drain was placed; closure was in layers with silkwormgut. A hasty examination of the liver and spleen, omentum and nodes showed no apparent metastases.

The time was forty-five minutes. The postoperative pulse was 92; the general condition was satisfactory. Recovery was uneventful except for the free sloughing of a portion of the abdominal wall. He went home on the thirty-ninth day in fair condition, with a fair appetite.

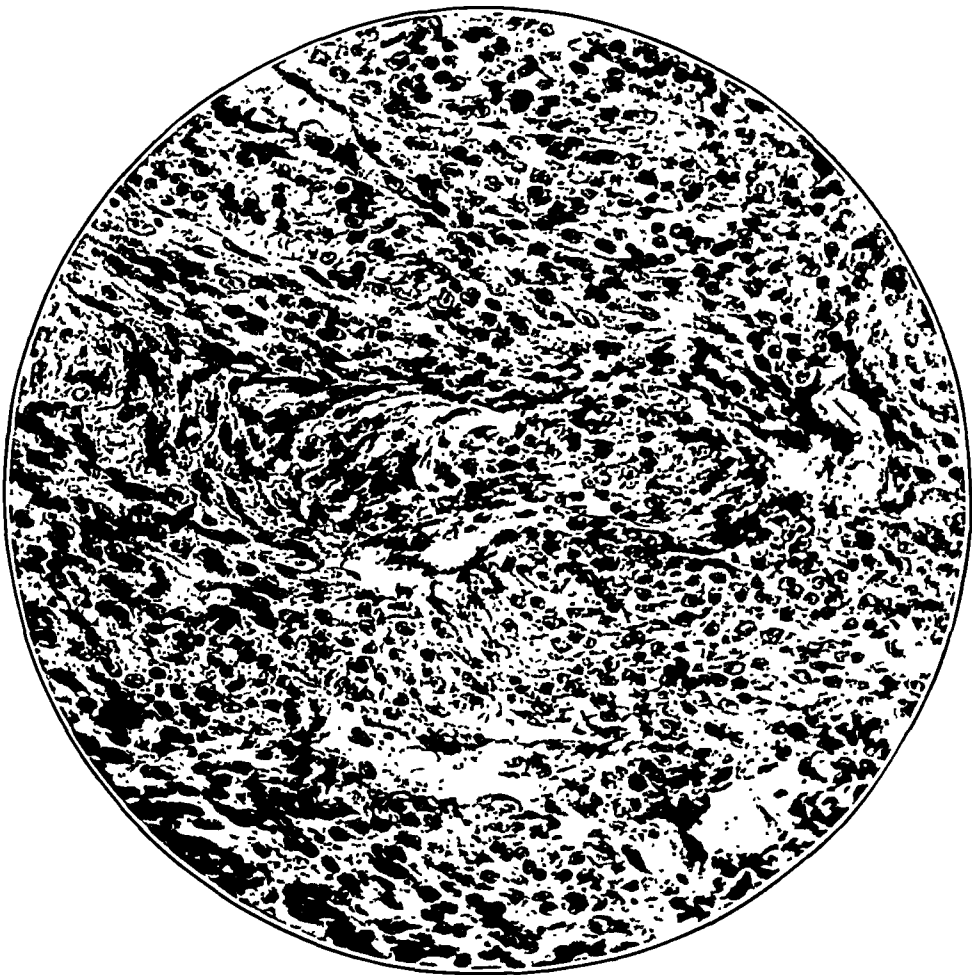


Fig. 3 (Case 2).—Perforating sarcoma of stomach in which resection was done.

The pathologist's report was that the tumor had a grayish white medullary appearance. Frozen sections showed a very cellular, actively growing tumor having the structure of a sarcoma.

Paraffin sections from various parts confirmed the previous diagnosis. The portion of the growth attached to the stomach had completely replaced the wall of the organ up to but not involving the mucosa or the muscularis mucosae. The margin of the tumor at this point was fairly sharply defined. The mucosa covering it showed the lesions of a chronic gastritis.

The tumor proper varied in appearance in different sections. In places it was very cellular, composed of spindle cells with large nuclei containing several

nucleoli, and resembling large nonstriated muscle fibers, though the cell bodies lacked the acidophilic properties of the latter. The cells showed numerous mitotic figures. In other regions the spindle cells were less numerous and were separated by areas of edematous tissue or large areas composed of a homogeneous material staining faintly with hematoxylin.

The follow-up reports were: October 8, the patient had gained 16 pounds (7.3 Kg.). He ate well, slept well, and had slight pain. November 19, the scar was firm; no tumor was felt, and the general condition was good. April 8, 1922, the patient, who had weighed 180 pounds (81.6 Kg.) at his best, now weighed 160 (72.6 Kg.). He ate everything and was working; no masses were felt. The wound bulged a little but there was no hernia. In June, 1922, there was a massive recurrence, which was hopeless. He was referred to the roentgen-ray department, Sept. 8, 1922, and given treatment at the Memorial Hospital. He died in January, 1923.

Deep roentgen-ray therapy was instituted on this man after the operation. He had a rather disagreeable reaction and refused to continue it.

CONCLUSIONS

Of the two cases of sarcoma of the stomach presented here, one, of the round cell type near the pylorus, closely resembled in its clinical aspects a calloused ulcer; the other, of the spindle cell type growing apparently from the musculature of the anterior wall of the stomach near the cardia, gave no clinical symptoms whatever until the day before operation. The patient with the round cell sarcoma who had a pylorotomy performed has made an apparently complete recovery and should be cured. The patient with the spindle cell tumor, whose operation was necessarily incomplete, relapsed after a year and died in less than two. On the whole the outlook in sarcoma of the stomach is fully as good as it is for carcinoma. If the diagnosis could be made earlier, the results, as in carcinoma, would probably be quite reasonably good.

PARTIAL TRACHEAL OBSTRUCTION

AN EXPERIMENTAL STUDY IN THE EFFECTS ON THE CIRCULATION
AND RESPIRATION OF MORPHINIZED DOGS *

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In the course of some observations on the blood gases in asthma,¹ certain findings indicated significant changes in the circulatory mechanism. Recently there has been an opportunity to make similar studies on two patients with acute laryngeal edema and interesting changes were found in the blood gases and blood reaction. Though the clinical studies have been temporarily abandoned because of a lack of material, the findings in asthma and acute laryngeal edema led to a series of controlled observations on experimental respiratory obstruction in dogs.

The problem was to study the effects of partial tracheal obstruction on the blood gases, blood reaction and volume flow. The object of the present article is to report the results of these experiments.

METHOD

Since asthma is difficult to produce in dogs and the experimental production of laryngeal edema is unsatisfactory, the following technic was employed to produce tracheal obstruction:

Dogs of from 6 to 14 kg. were used. The animals were given 0.06 gm. of morphin subcutaneously. Forty minutes to one hour later, tracheotomy was performed, local anesthesia being used when necessary. The carotid artery and the femoral vessels were exposed. A large metal cannula was inserted into the trachea and firmly tied so as to make an air tight connection. From the tracheal cannula a short rubber tube led to the mouthpiece of a Benedict spirometer filled with oxygen. The oxygen consumption was measured by the graphic method as described by Roth,² the Collins chronokymograph being used to record time on the

*From the departments of surgery, medicine and pathology of the Johns Hopkins University Medical Department.

1. Harrison, T. R., and Boyd, D.: Observations on the Blood Gases in Asthma, unpublished.

2. Roth, P.: Modifications of Apparatus and Improved Technique Adaptable to the Benedict Type of Respiration Apparatus, Boston M. & S. J. 166: 457 (April 6) 1923.

curve. By this method it was possible to obtain a constant oxygen consumption (Fig. 1) and at the same time a graphic record of the respiration.

After the animal had breathed quietly for about fifteen minutes, in order to insure a constant rate of oxygen consumption, blood samples were taken. Simultaneous samples of blood were withdrawn under oil from the right ventricle and the right femoral artery. At the same time a third observer drew blood from the left carotid artery into a tuberculin syringe for hydrogen ion determination. When the first observer experienced difficulty in puncturing the right ventricle, as was occasionally the case, the other two observers waited until venous blood appeared in the syringe before withdrawing arterial blood. In this way the three samples were obtained simultaneously. The pulse was counted before and after the punctures.

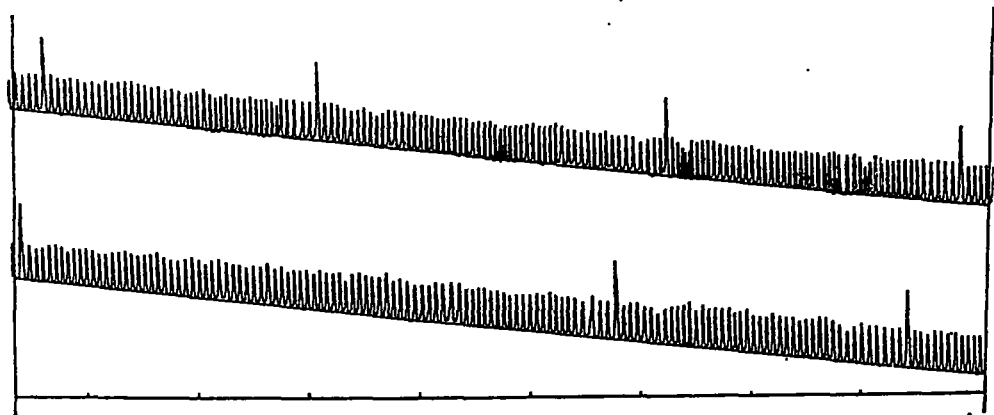


Fig. 1.—Normal respirations with even oxygen consumption. The curve passes from right to left. The rise in the curve indicates oxygen consumption. The tracing shows that the rate of rise is constant. The evenness of the respirations is noteworthy.

A small metal screw clamp was then placed over the rubber tube leading from the tracheal cannula to the mouthpiece of the Benedict apparatus. By turning the screw the tube could be constricted to any desired degree. In some experiments the effects of slight degrees of constriction were noted; in others the effects of greater constriction were observed. The degree of constriction could be measured by the degree of slowing of the respiratory rate and the curtailment of the respiratory excursion as seen on the kymographic record (Fig. 2).

Five or ten minutes after the respirations had reached a constant rate and depth, a second series of samples was drawn. The constriction was then released; and from thirty to sixty minutes later, when the animal had returned to normal, a third set of samples was taken.

At the end of each experiment the animal was killed with ether or chloroform and a necropsy was performed. The heart chambers were examined in order to make sure that the needle had not passed through the septum into the left ventricle, which would have resulted in mixing arterial and venous blood. The one experiment in which such a septum puncture was found was discarded in toto. The lungs also were examined. In one animal (Dog 8) which reacted in an entirely different manner from the others, a condition of pneumonic consolidation with

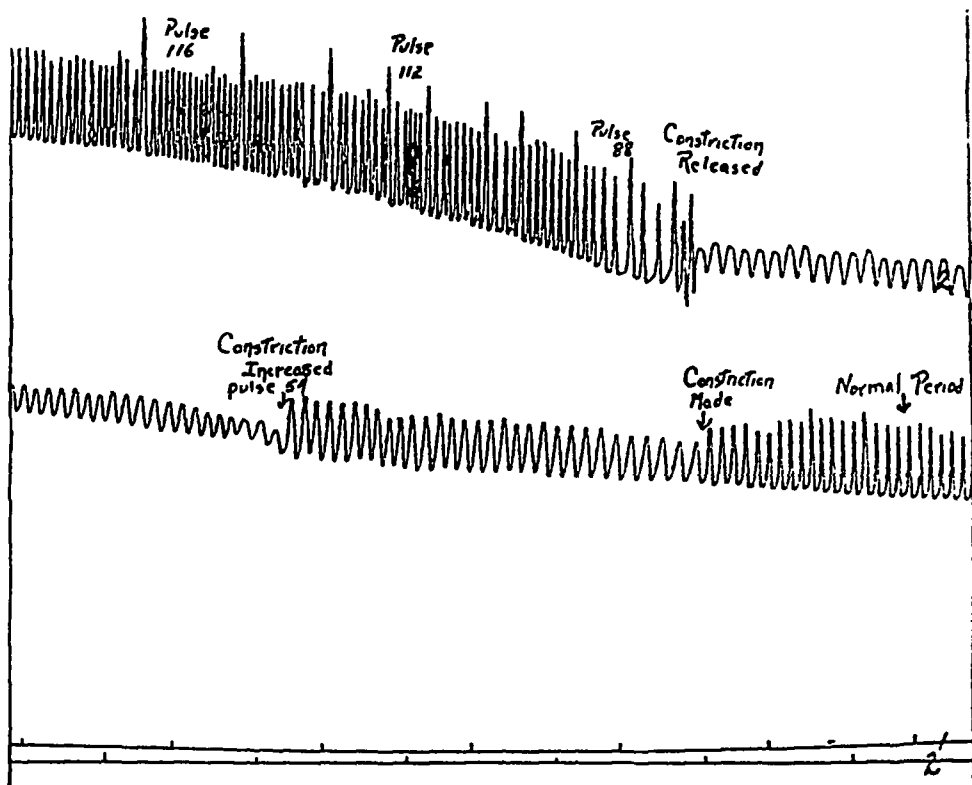


Fig. 2.—Effects of constriction on respiration and oxygen consumption. The curve passes from right to left. The effects of constriction and release on the respiratory rate and depth are striking. The oxygen consumption rate of rise of the curve is relatively constant.

pulmonary edema was found. In the other animals the lungs were normal except for hypostatic congestion and an occasional subpleural hemorrhage, which were due, we believe, to the asphyxial death.

The arterial and venous carbon dioxide and oxygen contents were determined by the method of Van Slyke and Stadie³ with the Van Slyke long bore constant pressure apparatus. The hydrogen ion concentra-

3. Van Slyke, D. D., and Stadie, W. C.: The Determination of the Gases of the Blood, *J. Biol. Chem.* 49:1 (Nov.) 1921.

tions were determined according to Hawkins' ⁴ modification of Cullen's ⁵ colorimetric method. A tuberculin syringe was used to measure the blood. Because of the nature of the experiments, these determinations had to be done hurriedly and a greater accuracy than $p_H \pm 0.03$ is not assumed. The changes encountered were always greater than these limits of error. In interpreting the results more emphasis has been laid on changes in p_H than on the actual p_H values. Since the Sorenson phenol red standards which were used are only satisfactory within the corrected range, p_H 6.90 to p_H 7.60, our more acid values are indicated in the tables by 6.90 —, and our greatest alkaline values by p_H 7.60 +.

The circulatory minute volume was calculated from the Fick principle:
$$\frac{\text{C.c. oxygen consumed per minute}}{\text{Amount of oxygen taken up by 1 c.c. of blood}} = \text{number of cubic centimeters of blood flowing through the lungs per minute.}$$
 The respiratory minute ventilation was calculated by multiplying the respiratory rate by the average respiratory depth as shown on the kymographic record.

RESULTS

The results of constriction were essentially the same in all animals except one. It was noted before the experiment that this dog had distemper and subsequent necropsy showed a bilateral bronchopneumonia. The figures obtained during the resting and constriction periods were entirely different from those in all other animals, and are not given in this article.

The values in the charts and tables for pulse and respiration rates, minute ventilation and oxygen consumption do not include those throughout each period, but only the figures at the times when blood samples were drawn.

Before Constriction.—The pulse rate was quite slow in all the animals, the average being less than 60 per minute. Cardiac irregularities were not observed in any case. The respirations were uniform in character in most instances, with the normal pause between inspiration and expiration. The respiratory rates ranged from 16 to 64 per minute, the high figure occurring in a large dog in which the respiratory center was stimulated rather than depressed by the morphin. The oxygen consumption varied almost directly with the weight of the animal under

4. Hawkins, J. W.: A Micromethod for the Determination of Hydrogen Ion Concentration in Whole Blood, *J. Biol. Chem.* **57**:493 (Sept.) 1923.

5. Cullen, G. E.: Studies in Acidosis, XIX, The Colorimetric Determination of the Hydrogen Ion Concentration of the Blood Plasma, *J. Biol. Chem.* **52**:501 (June) 1922.

observation and proceeded at a regular rate during the control period. The differences between arterial and venous oxygen and between venous and arterial carbon dioxide were within normal limits in all instances. The hydrogen ion concentration was less than 7.32 in every case owing to the fact that morphin produces a slight acidosis. The minute ventilation and the volume flow varied almost directly with the weight and as the pulse rates were quite uniform, the output per beat varied likewise.

Moderate Constriction.—When moderate constriction of the trachea was made, the following changes occurred in pulse rate, respiratory rate, oxygen consumption, blood gases, blood reaction and volume flow: The pulse rate increased slightly and the respirations were slowed and more labored. The animals used all the accessory muscles of respiration but did not open their mouths in gasping for breath, as did those with more

TABLE 1.—*Effects of Moderate Tracheal Obstruction (Average Figures for Five Experiments) **

Average weight of animals, 9.2 kg.

| | Pulse Rate | Respiration Rate | Oxygen Consumption per Minute, C.c. | Arterial Oxygen, per Cent. by Volume | Venous Oxygen, per Cent. by Volume | Venous CO ₂ , per Cent. by Volume | Arterial CO ₂ , per Cent. by Volume | p _H | Volume Flow, Liters | Output per Beat, C.c. |
|--|------------|------------------|-------------------------------------|--------------------------------------|------------------------------------|--|--|----------------|---------------------|-----------------------|
| Before constriction..... | 56 | 22 | 55.4 | 20.6 | 15.5 | 47.3 | 42.6 | 7.27 | 1.21 | 20.6 |
| During moderate tracheal constriction..... | 75 | 15 | 66.9 | 21.2 | 17.3 | 52.2 | 50.0 | 7.13 | 1.63 | 23.4 |
| Following release of constriction.. | 72 | 24 | 75.5 | 20.9 | 15.3 | 47.6 | 40.5 | 7.25 | 1.23 | 20.8 |

* In some of the experiments, all the functions listed were not determined. The figures in the table represent averages for the experiments in which determinations were made.

severe constriction. They did not struggle in any instance. The oxygen consumption increased despite the fact that the respirations were slow and shallow. This is shown in Figure 2. The rise in oxygen consumption seemed to be in proportion to the increased respiratory effort. The arterial oxygen was slightly higher with moderate constriction than during the control period. Anoxemia did not occur with this type of obstruction. There was a slight increase in the carbon dioxide content of both the arterial and the venous blood. The blood became more acid and the volume flow increased. The average figures giving the effects of the production of moderate tracheal obstruction in five animals are given in Table 1 and the effects on the respirations and oxygen consumption are shown in Figure 2.

Severe Constriction.—With severe constriction the following changes took place: The respirations became much more labored; the respiratory rate was slowed, and the respirations became shallower for the muscles of expiration did not seem able to empty the lungs completely. The

oxygen consumption was increased in all instances. The oxygen content of the arterial and venous blood tended to equalize and the carbon dioxide content was greatly increased. Whereas the arterial oxygen rose slightly with moderate constriction, there was a marked fall with severe constriction. The effects of severe constriction on the hydrogen ion concentration and blood flow were similar to those produced by moderate

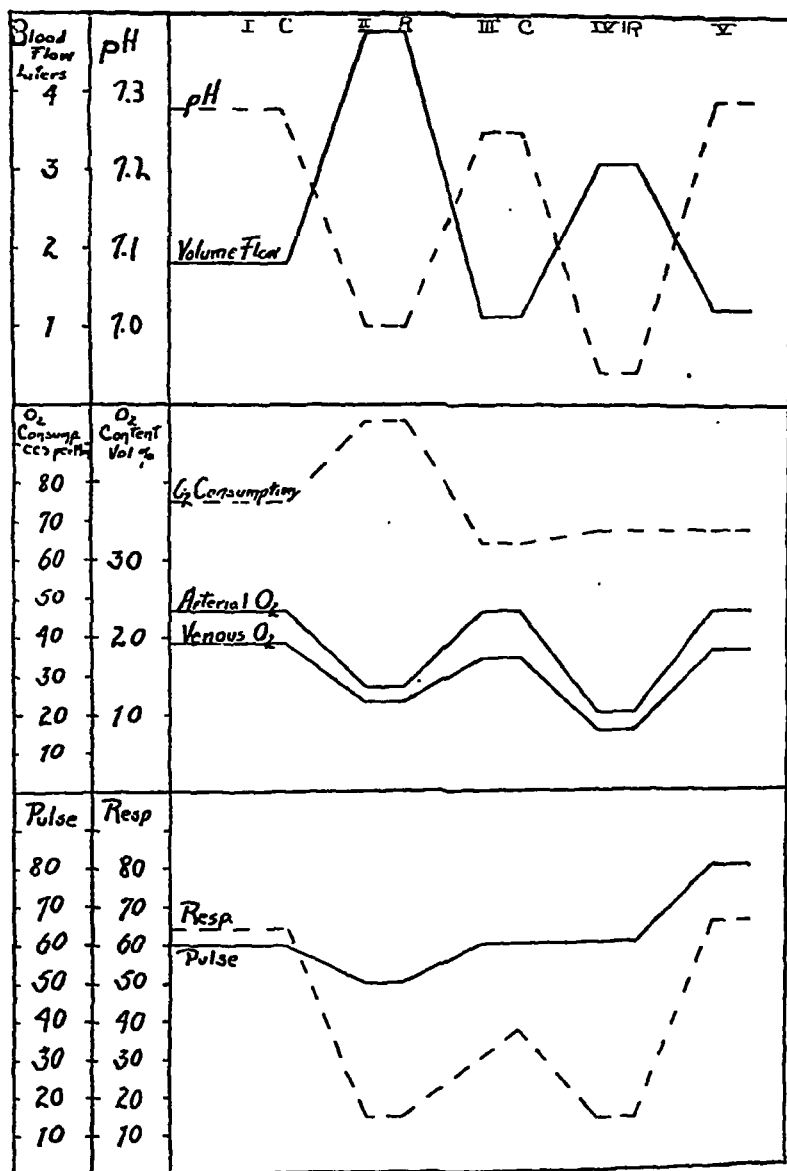


Fig. 3 (Experiment 11).—Effects of constriction; C, constriction; R, release. The striking changes that take place after partial constriction of the trachea, as shown in this chart, are: (1) immediate increase in the blood flow with a synchronous decrease in the pH of the blood; (2) a tendency for the curves for the oxygen content of the arterial and venous blood to approach one another at a lower level than normal, and (3) marked slowing of the respiratory rate.

obstruction but were of greater degree. The alkalinity of the blood was much diminished and the volume flow increased greatly. The results of severe constriction in a typical experiment are shown in Figure 3 and the average figures for four experiments are given in Table 2.

Release of Constriction.—When the constriction was released, the pulse rate usually increased together with the respirations and slowly returned to normal as the respirations became slower. The oxygen consumption increased suddenly on release of constriction but rapidly returned to normal (Fig. 2). The values for the blood gases, blood reaction and volume flow approached those obtained during the first control period. The complete figures for each individual experiment are given in Table 3.

TABLE 2.—*Effects of Severe Tracheal Obstruction (Average Figures for Four Experiments) **

Average weight of animals, 10.9 kg.

| | Pulse Rate | Respiration Rate | Oxygen Consumption per Minute, C.c. | Arterial Oxygen, per Cent. by Volume | Venous Oxygen, per Cent. by Volume | Venous CO ₂ , per Cent. by Volume | Arterial CO ₂ , per Cent. by Volume | p _H | Volume Flow, Liters | Output per Beat, C.c. |
|--|------------|------------------|-------------------------------------|--------------------------------------|------------------------------------|--|--|----------------|---------------------|-----------------------|
| Before constriction..... | 59 | 37 | 70.9 | 22.2 | 17.3 | 51.1 | 46.7 | 7.27 | 1.65 | 28.3 |
| During severe tracheal constriction..... | 59 | 18 | 79.3 | 12.2 | 9.9 | 67.2 | 66.5 | 6.98 | 3.58 | 68.2 |
| Following release of constriction.. | 88 | 31 | 67.8 | 22.3 | 17.0 | 51.5 | 45.8 | 7.25 | 1.31 | 15.4 |

* In some of the experiments, all the functions listed were not determined. The figures in the table represent averages for the experiments in which determinations were made.

Administration of Alkali.—Because of the fact that a decreased alkalinity of the blood was always associated with an increased volume flow, it was decided to alter the reaction of the blood by injecting alkali in order to study further the effect of the hydrogen ion concentration on the volume flow. Hence, in one animal in which partial tracheal obstruction had been produced, 45 c.c. of normal sodium bicarbonate was injected intravenously. The dyspnea was diminished immediately though the respirations were very shallow. The pulse rate did not change. The oxygen consumption was much lower but the arterial blood was normally saturated. The hydrogen ion concentration and circulatory minute volume returned to the normal level. The figures for this experiment are given in Table 4. The results are pictured in Figure 4. and it is of interest to contrast these with those in Figure 3.

TABLE 3.—*Effects of Partial Tracheal Obstruction on the Circulation and the Respiration**

| | Pulse Rate | Respiration Rate | Oxygen Consumption, per Minute, C.c. | Arterial Oxygen, per Cent. by Volume | Venous Oxygen, per Cent. by Volume | Venous CO ₂ , per Cent. by Volume | Arterial CO ₂ , per Cent. by Volume | <i>p_H</i> | Minute Ventilation, Liters | Volume Flow, Liters | Output per Beat, C.c. |
|---|------------|------------------|--------------------------------------|--------------------------------------|------------------------------------|--|--|----------------------|----------------------------|---------------------|-----------------------|
| Experiment 2 Weight, 9.5 kg. | | | | | | | | | | | |
| Before constriction.... | 45 | .. | | 20.4 | 14.3 | 52.5 | 49.5 | | | | |
| During mild constriction..... | 80 | .. | | 21.7 | 17.3 | 48.7 | 46.9 | | | | |
| One-half hour following release..... | .. | .. | | 20.3 | 15.4 | 51.9 | 48.5 | | | | |
| Experiment 4 Weight, 10 kg. | | | | | | | | | | | |
| Before constriction.... | 60 | 18 | | 18.9 | 13.2 | 46.3 | 39.1 | 7.24 | | | |
| During mild constriction..... | 96 | 18 | | 19.4 | 15.7 | 47.0 | 45.5 | 7.14 | | | |
| One and one-half hrs. following release.... | 90 | 36 | | 19.6 | 13.5 | 42.8 | 35.1 | 7.25 | | | |
| Experiment 5 Weight, 9.8 kg. | | | | | | | | | | | |
| Before constriction.... | 58 | 30 | | 18.0 | 11.8 | 53.3 | 48.7 | 7.28 | | | |
| During severe constriction..... | 60 | 13 | | 12.3 | 9.1 | 56.4 | 55.2 | 7.07 | | | |
| One-half hour following release..... | 30 | 22 | | 18.6 | 13.2 | 50.6 | 46.4 | 7.23 | | | |
| Experiment 6 Weight, 12.9 kg. | | | | | | | | | | | |
| Before constriction.... | 60 | 25 | 72.0 | 22.3 | 17.6 | 44.9 | 41.2 | 7.31 | | 1.53 | 25.5 |
| During constriction.... | 60 | 17 | 85.8 | 22.5 | 18.8 | 57.6 | 54.8 | 7.11 | | 2.32 | 38.7 |
| Three-fourths hour following release.... | 60 | .. | 96.5 | 22.3 | 17.1 | 49.5 | 45.0 | 7.24 | | 1.86 | 30.9 |
| Experiment 7 Weight, 6 kg. | | | | | | | | | | | |
| Before constriction.... | 57 | 22 | 42.0 | 21.6 | 16.9 | 42.1 | 36.2 | | 4.09 | 0.80 | 15.6 |
| During severe constriction..... | 72 | 9 | 59.1 | 21.9 | 17.8 | 53.0 | 51.0 | | 1.04 | 1.44 | 20.0 |
| One-half hour following release..... | 66 | 21 | 44.5 | 21.6 | 15.2 | 46.1 | 33.6 | | 4.63 | 0.69 | |
| Experiment 10 Weight, 9.1 kg. | | | | | | | | | | | |
| Before constriction.... | 56 | 15 | 61.6 | 24.4 | 21.1 | 45.2 | 39.5 | 7.25 | 4.80 | 1.90 | 34.0 |
| During severe constriction..... | 68 | 11 | 75.0 | 13.0 | 11.0 | 68.1 | 67.7 | 6.91 | 1.50 | 3.75 | 56.9 |
| One hour following release..... | 64 | 14 | 60.4 | 24.2 | 19.6 | 51.2 | 40.8 | 7.21 | | 1.35 | 21.1 |
| Experiment 11 Weight, 12.5 kg. | | | | | | | | | | | |
| Before constriction.... | 60 | 64 | 75.0 | 23.3 | 19.1 | 52.0 | 47.8 | 7.28 | 6.70 | 1.80 | 30.0 |
| During severe constriction..... | 50 | 15 | 96.0 | 13.6 | 11.6 | 74.1 | 71.4 | 7.00 | 1.13 | 4.80 | 96.0 |
| Three-fourths hour following release.... | 60 | 37 | 76.0 | 23.2 | 17.2 | 54.0 | 50.8 | 7.25 | 6.53 | 1.26 | 21.0 |
| Experiment 11 † | | | | | | | | | | | |
| Before constriction.... | 60 | 37 | 76.0 | 23.2 | 17.2 | 54.0 | 50.8 | 7.25 | 6.53 | 1.26 | 21.0 |
| During severe constriction..... | 60 | 14 | 67.0 | 10.1 | 7.9 | 70.3 | 71.5 | 6.94 | 1.59 | 3.10 | 51.7 |
| One hour following release..... | 100 | 49 | 67.0 | 23.2 | 18.1 | 50.0 | 42.2 | 7.29 | 6.95 | 1.31 | 13.1 |
| Experiment 19 Weight, 7.5 kg. | | | | | | | | | | | |
| Before constriction.... | 60 | 21 | 52.1 | 19.9 | 15.3 | 50.8 | 46.8 | 7.25 | 3.78 | 1.13 | 18.9 |
| During mild constriction..... | 68 | 15 | 55.9 | 20.7 | 17.0 | 54.6 | 51.7 | 7.14 | 2.72 | 1.51 | 22.2 |

* The figures are incomplete in Experiments 2, 4, and 5 as the animals were not breathing through a spirometer.

† After an interval of an hour, all the procedures in this experiment were repeated.

COMMENT

There are several theoretical objections to the method employed in these experiments: First, the use of anesthesia. As Henderson ⁶ points out, anesthesia may profoundly alter the volume flow. Morphin was used because Marshall ⁷ has found that morphin has no marked effect on the volume flow of the normal dog. Furthermore, the tables show that the final control blood flow was in nearly all instances of the same order of magnitude as the first control determination. This could not be true if morphin exerted any marked continuous depressant effect on the circulation. In such an instance the blood flow three or four hours after 1 grain (0.06 gm.) of morphin, would be distinctly lower than one hour after the administration of the drug.

TABLE 4.—*Effects of the Injection of Alkali When the Animal Has Partial Tracheal Obstruction*

Experiment 19; weight, 7.5 kg.

| | Pulse Rate | Respiration Rate | Oxygen Consumption, per Minute, C.c. | Arterial Oxygen, per Cent. by Volume | Venous Oxygen, per Cent. by Volume | Venous CO ₂ , per Cent. by Volume | Arterial CO ₂ , per Cent. by Volume | p _H | Minute Ventilation, Liters | Volume Flow, Liters | Output per Beat, C.c. |
|---|------------|------------------|--------------------------------------|--------------------------------------|------------------------------------|--|--|----------------|----------------------------|---------------------|-----------------------|
| Before constriction.... | 60 | 21 | 52.1 | 19.9 | 15.3 | 50.8 | 46.8 | 7.25 | 2.78 | 1.10 | 18.0 |
| During mild tracheal constriction..... | 68 | 15 | 55.9 | 20.7 | 17.0 | 54.6 | 51.7 | 7.14 | 2.72 | 1.51 | 22.2 |
| Shortly following injection of 45 c.c. normal sodium carbonate..... | 68 | .. | 38.5 | 19.0 | 15.3 | 46.0 | 40.8 | 7.21 | 1.82 | 1.04 | 15.0 |

Second, the effect of high oxygen tension. Lavorsier and Seguin ⁸ and, more recently, Benedict and Higgins ⁹ showed that the oxygen consumption is not increased by breathing pure oxygen. That the minute volume of blood is not altered is shown by a comparison of the results obtained by this method with those obtained by Marshall when the animals were breathing air. The values are given in Table 5.

However, the objection might be raised that obstruction to the respirations has a different effect when the animals are breathing pure oxygen instead of air. It was shown in parallel experiments that respiratory

6. Henderson, Y.: Volume Changes of the Heart. *Physiological Rev.* 3:165 (April) 1923.

7. Marshall, E. K., Jr.: Personal communication to the authors.

8. Lavoisier and Seguin: *Second Memoir sur le Respiration les Animaux*. *Ann. de Chem.* 41:318, 1814.

9. Benedict, F. G., and Higgins, H. L.: Effects on Man at Rest of Breathing Oxygen-Rich Gas Mixtures, *Am. J. Physiol.* 23, 1911

obstruction affects the blood gases in the same manner, regardless of whether air or oxygen is breathed. In both instances a slight degree of constriction causes moderate carbon dioxid retention but no anoxemia, whereas extreme degrees of obstruction cause great carbon dioxid retention and anoxemia. These figures are given in Table 6.

The important results of respiratory obstruction that were found in these experiments include: (1) acidosis; (2) increased blood flow with

TABLE 5.—*Effect of Morphin and Oxygen on the Blood Flow*

| Results Obtained by Dr. E. K. Marshall, Jr., on Unanesthetized Dogs * | | Results Obtained by Authors on Dogs Anesthetized with Morphin and Breathing Oxygen | | | |
|---|--|--|--|------------|--|
| Dog Number | Volume Flow per Minute per Kilogram, C.c. | Dog Number | Volume Flow per Minute per Kilogram, C.c. | Dog Number | Volume Flow per Minute per Kilogram, C.c. |
| 1 | 109 | 6 | 119 | 15 | 147 |
| 2 | 122 | 7 | 148 | 16 | 209 |
| 3 | 154 | 10 | 210 | 17 | 155 |
| 4 | 154 | 11 | 144 | 18 | 170 |
| | | 12 | 151 | 19 | 151 |
| | | 14 | 153 | | |
| Average..... | 135 | | | | 159 |

* Dr. Marshall very kindly furnished the figures for his normal dogs. His values for each animal represent the average of a number of determinations. Our figures represent only one determination on each animal. It can be seen that there is no great difference, the values for the trained animals being only slightly lower than those for the morphinized animals.

TABLE 6.—*Similarity of Blood Gases Following Mild and Severe Constriction When (1) Air Is Breathed and (2) Pure Oxygen Is Used*

| Ex- peri- ment Num- ber | Gas Breathed | Degree of Con- stric- tion | Arterial Oxygen, per Cent. by Volume | | | Venous Oxygen, per Cent. by Volume | | | Arterial CO ₂ , per Cent. by Volume | | | Venous CO ₂ , per Cent. by Volume | | |
|-------------------------------------|-----------------|-------------------------------------|--|---------------------------------------|---------------------------------|--|---------------------------------------|---------------------------------|--|---------------------------------------|---------------------------------|--|---------------------------------------|---------------------------------|
| | | | Be- fore Con- stric- tion | Dur- ing Con- stric- tion | After Con- stric- tion | Be- fore Con- stric- tion | Dur- ing Con- stric- tion | After Con- stric- tion | Be- fore Con- stric- tion | Dur- ing Con- stric- tion | After Con- stric- tion | Be- fore Con- stric- tion | Dur- ing Con- stric- tion | After Con- stric- tion |
| 4 | Air | Mild | 18.9 | 19.4 | 19.6 | 13.2 | 15.7 | 13.5 | 39.1 | 45.5 | 35.1 | 46.3 | 47.0 | 35.1 |
| 6 | Oxygen | Mild | 22.3 | 22.5 | 22.3 | 17.6 | 18.8 | 17.1 | 41.2 | 54.8 | 45.0 | 44.9 | 57.6 | 49.5 |
| 5 | Air | Severe | 18.0 | 12.3 | 18.6 | 11.8 | 9.1 | 13.2 | 48.7 | 55.2 | 46.4 | 53.3 | 56.4 | 50.6 |
| 10 | Oxygen | Severe | 24.4 | 12.0 | 24.2 | 21.1 | 11.0 | 19.6 | 39.5 | 67.7 | 40.8 | 45.2 | 68.1 | 51.2 |

a pulse rate that was almost constant; (3) a tendency for the oxygen content of the arterial and venous blood to equalize at a lower level than normal; (4) an increase of the carbon dioxid content of the arterial and venous blood, and (5) marked slowing of the respiratory rate and the diminished minute ventilation. These points together with the effects of the injection of alkali when obstruction was present are discussed as follows:

1. *Acidosis*.—Obstruction to the respirations invariably caused an acidosis that was dependent on the retention of carbon dioxid. The

usual types of acidosis seen clinically—diabetic and renal—are not due to an excess of carbon dioxide but to an excess of nonvolatile acids. In these conditions the carbon dioxide is blown off as a compensatory mechanism and the amount of the gas in the blood is decreased; whereas in the acidosis of respiratory obstruction the carbon dioxide content is increased. This emphasizes the point that has been so frequently made

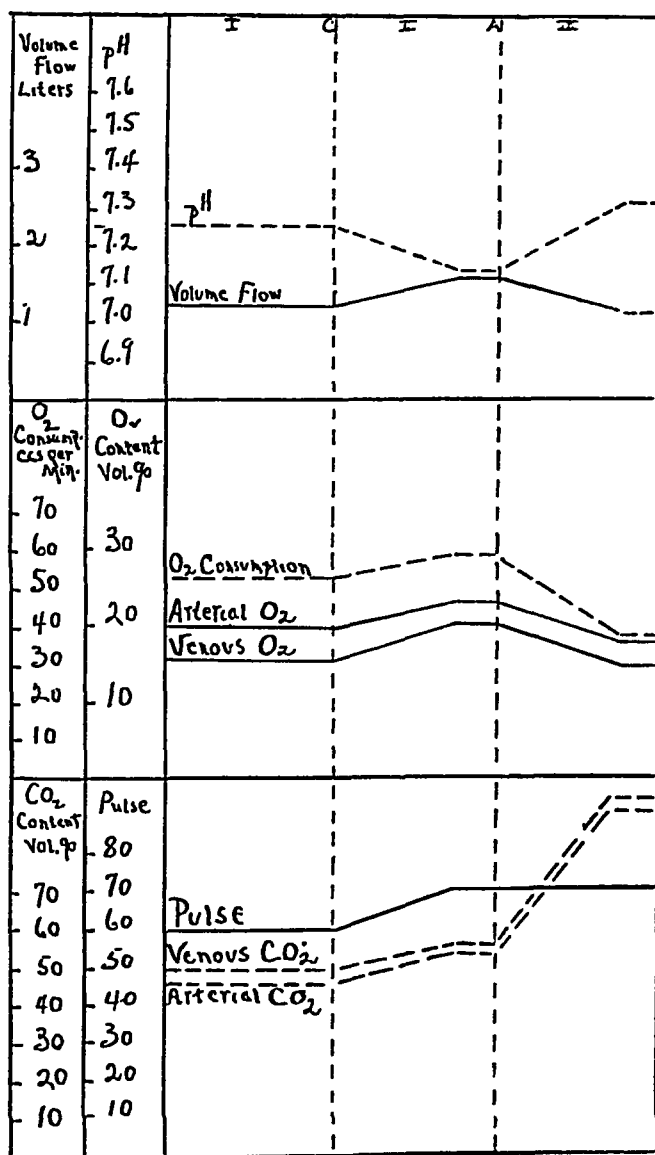


Fig. 4 (Experiment 19).—Effects of injection of alkali when partial tracheal obstruction is present; C, constriction; A, alkali injection. The changes that take place when alkali is injected intravenously into an animal that has partial tracheal obstruction are: (1) the immediate decrease in the blood flow with a synchronous increase in the pH of the blood; (2) a decrease in oxygen consumption though the arterial blood remains normally saturated, and (3) a marked increase in the carbon dioxide content of the arterial and venous blood.

by Van Slyke,¹⁰ that the carbon dioxid combining power (or content) of the blood is not an invariable index of the hydrogen ion concentration.

2. *Increased Blood Flow.*—The volume flow frequently increased as much as 100 per cent. when tracheal constriction was produced and in several instances a much greater rise was noted. This is not entirely in accord with the observations of Huggett,¹¹ who found that an inspiratory resistance caused an increased flow, whereas an expiratory resistance decreased the flow. This discrepancy can probably be explained by the fact that Huggett worked with cats—weaker animals than dogs—and used urethan as an anesthetic. Marshall has shown that urethan alters the circulatory mechanism.

The fact that a normal respiratory mechanism can compensate for an impaired circulation is well recognized. From these experiments one is led to believe that the normal circulation can to a great extent compensate for a failing respiration. When the alveolar tension of carbon dioxid is increased and the alveolar tension of oxygen is diminished, each unit of blood can take up less oxygen and give off less carbon dioxid. Hence, if the total exchange of these gases is to remain unaltered, the number of units of blood passing through the lungs must be increased. The circulation offers the second line of defense against failure of tissue metabolism.

Since respiratory obstruction caused both an acidosis and an increased blood flow, the question naturally arose as to whether the first phenomenon was the cause of the second. This point has been investigated in some detail in another series of experiments which are to be reported elsewhere.¹²

3. *Effect of Respiratory Obstruction on the Absorption of Oxygen and Excretion of Carbon Dioxid.*—With slight degrees of obstruction there was no effect; with moderate degrees of obstruction carbon dioxid retention and acidosis were produced but anoxemia was not found. This was true regardless of whether the animals were breathing oxygen or air (Table 6). With extreme obstruction marked acidosis and anoxemia occurred. Even in the latter instance the oxygen consumption was not decreased. These findings are noteworthy in view of a recent tendency to emphasize the stability of the carbon dioxid mechanism as

10. Van Slyke, D. D.: Studies of Acidosis, XVII, The Normal and Abnormal Variations in the Acid-Base Balance of the Blood, *J. Biol. Chem.* 48:153 (Sept.) 1921.

11. Huggett, A. S.: Studies on the Respiration and Circulation of the Cat, IV, The Heart Output During Respiratory Obstruction, *J. Physiol.* 59:373 (Dec.) 1924.

12. Harrison, T. R.; Wilson, C. P., and Blalock, A.: The Effects of Changes in Hydrogen Ion Concentration on the Circulatory Minute Volume in Morphinized Dogs, unpublished.

contrasted with the oxygen mechanism. Thus, Hastings, Neill, Morgan and Binger¹³ state:

In any individual breathing ordinary atmosphere, respiratory hindrance must result in serious anoxemia long before carbon dioxid acidosis has become at all significant.

This conclusion is drawn from work on pneumonia. In this condition the normal lung may, by overventilation, compensate for lack of carbon dioxid excretion in the diseased lung, but cannot compensate for lack of oxygen absorption because the blood through the good lung is already nearly 100 per cent. saturated. With obstruction to the respirations quite a different condition exists. The tension of oxygen in the alveoli may fall by as much as 35 per cent. before anoxemia occurs, but a slight rise in alveolar carbon dioxid tension, uncompensated by overventilation, causes acidosis. Under such conditions the oxygen mechanism is the more stable. That this is also true under normal conditions is evidenced by the work of Burwell and Robinson,¹⁴ who found that the rate of blood flow, determined by the oxygen method, was distinctly less variable than when determined by the carbon dioxid method.

Our findings are in accord with the observations of Hoover,¹⁵ who states:

Cyanosis does not follow even very severe stenosis of the trachea. It is an impressive fact that a patient may have uncomplicated stenosis of the trachea which will compel the use of the utmost strength for both inspiration and expiration and still show no visible evidence of anoxemia.

4. *Diminished Minute Ventilation.*—Obstruction to the respirations decreases the amount of air that can be breathed in one respiration, and increases the amount of time necessary to inhale or exhale a given amount. Under such conditions rapid, shallow breathing is extremely inefficient because a great part of the expiratory effort is expended in washing the dead space; hence it seems that slow respirations of the greatest possible depth are more efficient than shallow respirations at a more rapid rate.

In the animals with respiratory obstruction, the respirations were actually slow and observation of the animals gave the impression that the greatest possible effort was being expended with each expiration and inspiration.

13. Hastings, A. B.; Neill, J. M.; Morgan, H. J., and Binger, C. A. L.: Blood Reaction and Blood Gases in Pneumonia, *J. Clin. Investigation* 1:125, 1924.

14. Burwell, C. S., and Robinson, G. C.: The Gaseous Content of the Blood and the Output of the Heart in Normal Resting Adults, *J. Clin. Investigation* 1:87, 1924.

15. Hoover, C. F.: *Nelson's Loose Leaf Living Medicine*, Thomas Nelson and Sons, \$:393.

The question as to why the respiratory mechanism should function in the most efficient manner under these conditions, is of some interest. We believe that this can be partially accounted for by the acidosis, which is usually characterized clinically by hyperpnea rather than polypnea. However, it is possible that the Hering-Brauer reflex enters into this mechanism and, since no experiments were done with the vagi cut or frozen, this point is not definitely settled.

5. Effect of Alkali When Obstruction Is Present.—Since acidosis is one of the most striking effects of obstruction, the question naturally arises as to the possibility of beneficial effects from alkaline therapy.

In the one animal to which alkali was given during the period of respiratory obstruction, rather striking effects were obtained. The respirations were greatly diminished and the animal no longer appeared dyspneic; the blood flow returned to the normal level. However—and this seems to be an important fact—the oxygen consumption was decreased. Alkali depressed the respirations so much that the intake of oxygen became subnormal.

These findings indicate that whereas beneficial results may be expected clinically from giving alkali to patients with respiratory obstruction due to inoperable causes, the administration should be carried out very cautiously and slowly. Furthermore, since alkali, being a respiratory depressant, greatly diminishes the minute ventilation, it is desirable to have the air breathed rich in oxygen. Therefore, alkaline therapy should not be attempted unless oxygen is also given.

If suitable cases of respiratory obstruction are encountered in the future, we plan to make a clinical study of the effects of administering alkali. From the present data no very definite conclusions can be drawn. However, it is suggested that such therapy may prove valuable in diphtheria and in cases of moderately severe laryngeal edema such as sometimes follow bronchoscopy. In such cases tracheotomy is undesirable, and we believe that it may be avoided in some instances by the giving of alkali and oxygen. This treatment may prove of palliative value in the severe paroxysms of dyspnea in cases of mediastinal aneurysm or in tumor pressing on the trachea.

SUMMARY AND CONCLUSIONS

Obstruction to the respirations has been produced in dogs, anesthetized with morphin. The pulse rate, respiratory rate, minute ventilation, oxygen consumption, arterial and venous oxygen and carbon dioxide contents, hydrogen ion concentration, and circulatory minute volume have been studied. The following results have been obtained:

1. Partial obstruction of the tracheal cannula caused slow, shallow breathing.

2. An increase of the carbon dioxide content of the arterial and venous blood occurred with moderate degrees of obstruction, whereas anoxemia did not occur until the obstruction became extreme.

3. Even with extreme degrees of obstruction, the oxygen consumption was not decreased.

4. Acidosis, due to the accumulation of carbon dioxide, was a constant finding.

5. The circulatory minute volume was very much increased although the pulse rate was practically unchanged.

6. In one animal to which alkali was given intravenously during the period of tracheal obstruction, the hydrogen ion concentration and blood flow became normal but the minute ventilation and oxygen consumption were decreased below the normal values. The dyspnea appeared to be relieved. From these observations the following conclusions are drawn:

(a) A healthy circulation may partially compensate for a failing respiratory mechanism.

(b) When the lungs are normal and tracheal obstruction is produced, the carbon dioxide content of the blood is elevated quite markedly before anoxemia occurs.

(c) Alkaline therapy may be of value in cases of tracheal obstruction due to inoperable causes and in laryngeal edema following instrumentation. Whenever alkali is administered, oxygen should also be given.

POSTOPERATIVE COLONBACILLURIA*

INCIDENCE IN ONE HUNDRED AND THIRTY CASES FOLLOWING SURGICAL PROCEDURES

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The appearance of the colon bacillus in the urinary tract in health following gestation, disease or injury, and especially following surgical operation, is a problem of peculiar interest to the profession.

When the colon bacillus was first isolated from human feces by Emmerich in 1885 he thought it to be the specific cause of Asiatic cholera but, later, it was found to be a normal habitant of the feces. However, its presence in appreciable numbers in uncontaminated urine has usually been considered as associated with pathologic change, for the urinary tract is not considered the natural locality of the colon bacillus.

In searching the literature one is impressed with the variant conditions during or following which a colonbacilluria exists, aside from certain saprophytic strains occurring in apparently normal subjects. It is quite commonly intercurrent in the infectious diseases. Colon bacillus pyelitis frequently complicates the diseases of childhood. Such diversified conditions as accidental injury with external lacerations, general run down state due to overwork, and cyluria (caused apparently by *Filaria sanguinis-hominis*) have been accompanied or followed by a colon bacillus infection of the kidneys.

Obstetricians and gynecologists always have been confronted with complications due to urinary tract infection, and since the discovery of the colon bacillus different strains of this organism are found in a rather large majority of cases as the predominating or the only infecting agent. Often the general surgeon is faced with a laboratory report that suggests infection of the urinary system, and in this study we have embodied the incidence and significance of colonbacilluria following surgical operations.

Severe infections of the upper urinary tract such as pyelonephritis or pyelocystitis are not altogether uncommon after operative procedure. Usually bacilli of the colon group are found as the cause. It may be that they overgrow and crowd out a primary invader, such as the

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staphylococcus or the streptococcus. Stirling¹ thinks that if careful search is made an organism other than the colon bacillus may be isolated in certain cases. In his series of 175 cases of pyelonephritis, 13 per cent. followed surgical operations.

VIRULENCE

Many are of the opinion that patients recover from the subjective symptoms of pyelitis after a few days in bed but continue excreting large numbers of colon bacilli in the urine. Meyer-Betz² hints that the body, accustomed to the parasitism of *Bacillus coli* in the intestines from birth, adapts itself to the urinary inhabitant through an acquired general immunity or an acquired capacity of the mucosa of the renal pelvis to prevent passage of *Bacillus coli* into the blood.

Persistent colonbacilluria without symptoms is a phenomenon that is not uncommon. Graff³ believes that after colon bacilli have reached the renal pelvis, bacteriuria may be present for weeks, months or years without causing symptoms. He emphasizes the constant danger that some special circumstance may be the exciting cause of an acute infection with marked subjective and objective symptoms. Koll⁴ in 1915 expressed the view that saprophytic bacteria do not exist in the upper urinary system but are found only in the urethra and the prostate. Hess,⁵ in his experimental work, caused rabbits to pass *Bacillus coli* rapidly through the kidneys without producing lesions.

Different opinions are held as to the virulence of *Bacillus coli* in the urinary tract. Many authorities believe that it varies within rather wide limits. Keyes⁶ holds that it is only mildly noxious in the upper urinary tract. The existence of the many strains of this organism probably explains in part its varying pathogenic status in the urinary system. The importance of the local and general resistance of the individual to the colon bacillus in the urinary tract should not be overlooked. Barney⁷ has observed several cases in which a state of low resistance due to overwork seemed to be an important etiologic factor.

1. Stirling, W. C., Jr.: Observations on 175 Cases of Pyelonephritis, Surg., Gynec. & Obst. **37**:751 (Dec.) 1923.

2. Meyer-Betz, F.: Über Primäre Colipyelitis, Deutsch. Arch. f. klin. Med. **105**:531, 1912.

3. Graff, H.: Die Koliinfektion der Nieren und ihre Behandlung, Ztschr. f. urol. Chir. **3**:6-32, 1914.

4. Koll, I. S.: Bacteria of the Urinary Organs, Not Including the Tubercle Bacillus, Internat. Abstr. Surg. **20**:349 (April) 1915.

5. Hess, Otto: Experimentelle Untersuchungen über die Bacterium Coli Infektion der Harnwege, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **26**:135, 1913.

6. Keyes, E. L.: Diseases of the Genito-Urinary Organs, New York, D. Appleton & Co., 1913, pp. 328-337.

7. Barney, J. D.: Acute Colon Bacillus Infections of the Urinary Tract, J. A. M. A. **71**:1642 (Nov. 16) 1918.

ETIOLOGIC FACTORS IN GENERAL

Thompson-Walker⁸ and others point to the intestinal tract with conditions such as protracted constipation or severe diarrhea as the source of the organism in the urine. Rawls⁹ reported fourteen cases of urinary tract infection due to the colon bacillus occurring after operation, and accounted for the primary foci in six different localities as follows: infected ectopic gestation and abdominal wound; appendiceal and pelvic abscess; carcinoma of the stomach and gallbladder; appendix alone; pelvic abscess, and perinephritic abscess.

The incidence of colonbacilluria among women is greater than among men and the female sex also predominates in the number seeking treatment because of urinary tract symptoms. Sterling¹ points out that one reason for this condition is doubtless lack of drainage in the female urinary system because the generative organs encroach to a greater or lesser extent on the urinary tract. Baisch¹⁰ found that when women were confined to bed and were allowed to void only twice in twenty-four hours *Bacillus coli* invariably could be cultivated from the external urethra and its vicinity within five days. Cabot¹¹ found colon bacilli in the urine in about 25 per cent. of a series of cases studied during pregnancy.

The right kidney and ureter are involved more often than the left. Kretschmer¹² cited Franke, who was able by injecting the lymphatics of the large bowel to show that the lymphatics of the right side pass over the right kidney capsule. Franke concluded that there exists on the right side and probably on the left a direct communication between the large bowel and the kidney by way of the lymphatics. Kretschmer maintained that constipation is one of the primary predisposing causes of pyelitis, explaining that the colon bacilli arrive in greater numbers after their increased production in the bowel. He noted the large number of cases of pyelitis found in follicular enteritis and cited Tavel's postoperative goiter case in which the wound became infected with *Bacillus coli*, the patient having had a severe attack of gastro-enteritis. He also cited Asch's four cases of bacillus coli infection of the urinary

8. Thompson-Walker, J. W.: Acute Pyelitis, Pyelonephritis and Suppurative Nephritis, Practitioner 36:655, 1911.

9. Rawls, R. M.: B. Coli Infections of the Urinary Tract, M. Rec. 81:359 (Feb. 24) 1912.

10. Baisch, A.: Ztschr. f. Geburtsh. u. Gynäk. 8:124, 1904.

11. Cabot, H.: The Rôle of the Colon Bacillus in Infections of the Kidney, New York State J. Med. 21:35 (Feb.) 1921.

12. Kretschmer, H. L.: Pyelitis of Pregnancy, J. A. M. A. 81:1585 (Nov. 10) 1923.

tract cured by treating the associated constipation. Français,¹³ in three cases of renovesical colon bacillus infection due to cecal stasis, went so far as to treat by operation (colostomy and ileocolostomy) the cause of the stasis, reporting a disappearance of the bacilluria and complete alleviation of the urinary symptoms. On the other hand, Hess,⁵ in his extensive animal experimentation, produced fecal stasis through opium administration for a period of more than three months with simultaneous constriction of one ureter, and at necropsy found no microscopic lesions in the urinary tract, *Bacillus coli* being present only in the intestinal tract.

The different theories advanced as to the effect, directly or indirectly, of surgical operation on *Bacillus coli* infections of the urinary tract are an interesting phase of this subject. Furniss¹⁴ pointed to wounds infected with intestinal contents as a potential source of urinary tract infection. He laid stress on his belief that renal infections are often caused by the breaking loose from the wound region of infected thrombi that reach the kidney by the hematogenous route, and observed the process as a sudden, acute condition occurring several days after the operation. In his experience operations on the intestinal canal also predispose to urinary tract infection. He believed that many cases occurred in which there never had been any antecedent catheterization, cystitis or other infection of the urinary system.

In a logical discussion of the reasons for postoperative urinary tract infection, Jacobson and Keller¹⁵ point out certain unanatomic conditions remaining after operations in which portions of the urinary tract are distorted. Trauma and congestion with interruption of the blood supply follow all operations in which the urinary bladder is separated from its attachments. In their experience cystoscopic examination following such operations often revealed anatomic malposition of the base, distortion of the trigon, displacement of the ureteral orifices and swelling with edema about the urethral orifice. Often pockets are left in the bladder which are seldom free from residual urine.

Of vital importance in the etiology of urinary infection, possibly of more importance than the presence of the organisms, is that condition of the urinary tract which has been referred to by different authorities as the "prepared soil." Keyes⁶ described those factors, which usually follow one another in rapid sequence, as obstruction (due to prostate,

13. Français, H.: J. d'urol. méd. et chir. **16**:425, 1923; abstr., Surg. Gynec. & Obst. **38**:442 (May) 1924.

14. Furniss, H. D.: Postoperative Renal Infection, J.A.M.A. **61**:957 (Sept. 20) 1913.

15. Jacobson, J. H., and Keller, J. G.: Postoperative Retention of Urine and Cystitis, J. A. M. A. **57**:1981 (Dec. 16) 1911.

stricture, stone or tumor) followed by retention, congestion and vascular changes, stretching and atony of the bladder with consequent residual urine, and the addition possibly of trauma. Here the preparation is complete for bacterial invasion. He declares that no other organism except the tubercle bacillus and the gonococcus can take root and multiply in the urinary tract unless the soil on which they flourish is congested, and asserts that bacteria are not the most essential agents in infection of the urinary tract.

Cabot ¹⁶ in his well known monograph "The Doctrine of the Prepared Soil" has followed a very similar line of reasoning. He considers post-operative congestion of the whole urinary tract coupled with low resistance to the colon bacillus typical preparation of the soil, which will usually be followed by a flourishing growth of the organisms present. Such congestion he says, is often due to retention, which is followed in turn by distention and often by sudden emptying of the bladder by catheterization of the patient.

In 1911 Brewer ¹⁷ published some of the results of his animal experimentation, in which he observed in part the effect of more or less complete anemia, hyperemia and other vascular changes in lowering the resistance of the kidney to blood infection. He found that such changes in the blood supply so lowered the resistance of the organ as to result in definite surgical lesions.

Trauma is regarded as a most important element in the causation of urinary tract infections when organisms such as *Bacillus coli* are present. Koll ¹⁸ in 1915, after experimental work on animals, reported that the nontraumatized kidney in the absence of obstruction usually overcomes spontaneously the invasion of virulent micro-organisms. Traumatic injury with the organisms present may not be always a certain exciting factor, however, for certain observers have found the urinary tract capable of protecting itself against invading micro-organisms, especially the colon bacillus, even in the presence of trauma, provided no other factors such as obstruction are coincident. Barber and Draper ¹⁹ concluded after a series of experiments on animals that traumatism of the ureter results in a mechanically changed kidney that may be infected later.

16. Cabot, H.: Doctrine of the Prepared Soil, *Canad. M. A. J.* **81**:610 (Sept.) 1921.

17. Brewer, G. E.: Observations on Acute Hemic Infections of the Kidney, *Am. J. Urol.* **19**:549 (Dec.) 1913.

18. Koll, Irwin S.: The Experimental Effect of the Colon Bacillus on the Kidney, *J. A. M. A.* **64**:297 (Jan. 23) 1915.

19. Barber, W. H., and Draper, J. W.: Renal Infections, *J. A. M. A.* **64**:205 (Jan. 16) 1915.

Obstruction is conceded by practically all to be directly or indirectly the most important factor in preparing the urinary system for bacterial invasion, and this leads us to a consideration of the part played by residual urine. Curtis²⁰ has made careful observations on the management of stasis of vesical urine, especially in the female bladder, and has pointed out repeatedly the great increase in the danger of infection of the urinary tract wherever there are postoperative accumulations of residual urine. In 1923 he found in a series of 1,595 convalescent female patients that residual urine of more than an ounce (30 c.c.) was present after a return to spontaneous micturition in more than 64 per cent. of all repeatedly catheterized patients. The residual urine is the chief cause of infection.

Falls²¹ noted *Bacillus coli* in six out of ten cases of residual urine specimens collected from pregnant women. Albeck²² reported after examination of 250 gynecologic cases that 130 presented bacteriuria. Of the group of 120 without residual urine only sixteen showed bacteriuria, the remaining 104 being sterile. In this series no case of urinary obstruction was present but the bladder had been weakened by age, tumors or displacements.

Mills²³ pointed out the effect of gravity in subjects who have residual urine, describing the funnel shape of the bladder with the apex corresponding to the urethra as shown by the roentgenograph with a bismuth suspension. This observer found that the bismuth suspension in the bladder would not wash out with the patient in the reclining position but that in the sitting position complete evacuation could be accomplished. Furthermore, the wide variation in amounts of urine collected by the catheter in certain of the cases at regular intervals, indicate clearly that the catheter could not be relied on completely to empty the bladder. Some chronically distended bladders with lateral pouches would be very difficult to empty completely. In all cases with residual urine, he found bacilluria very common.

Regarding the importance of the catheter as a factor in bladder infections there is some divergence of opinion. Certain clinicians concur in the opinion that some cases of bladder infection are held to be due to catheterization in which this procedure is not the cause. Curtis²⁰

20. Curtis, A. H.: Management of the Female Urinary Bladder After Operation and During Pregnancy, J. A. M. A. 80:1126 (April 2) 1923.

21. Falls, F. H.: A Contribution to the Study of Pyelitis in Pregnancy, J. A. M. A. 81:1590 (Nov. 10) 1923.

22. Albeck, F.: Untersuchungen über die Funktion der Weiblichen Harnblase bei Frauen Krankheiten, Monatschr. f. Geburtsh. u. Gynäk. 38:585, 1913.

23. Mills, R. G.: Incidence of Postoperative Catheterization, Ann. Surg. 79:813 (June) 1924.

led to a perfect recovery without any subsequent fistulas and with satisfactory final function of both kidneys.

Renal Neoplasm.—Cabot¹⁰ states that the incision or incisions for the exposure of renal tumors must give free access and handicap the surgeon as little as is compatible with a decent respect for anatomic structures. The incision must also allow a wide exposure of the perirenal structures because in many, if not most, of the cases it will be necessary to deal with something more than the kidney itself. The surgeon should do his work with as little permanent damage as possible. Damage to the nerve supply, particularly in the case of operations involving divisions of the abdominal wall, is to be avoided if possible. Division of muscular structures, though it often looks serious and gives the impression of radicalism, is not so in fact. Muscular structures unite with fibrous tissue giving a scar of satisfactory firmness and doing little damage to the general integrity of the abdominal wall. The classical oblique incision ordinarily begins at about the anterior border of the erector group of lumbar muscles and extends forward and downward just below and, in general, parallel with the twelfth rib. It is possible to extend this incision forward and inward to almost any extent. This incision avoids damage to large nerve trunks and has been eminently satisfactory for a large majority of the problems presented in renal surgery. In the case of renal tumors, however, it does not give quite satisfactory access to the tumor. In many of these cases the mass is situated relatively high under the diaphragm. It is necessary to remove not only the kidney itself but also its fat capsule, a requirement that does not obtain in other operations on the kidney. The most important defect of this incision, however, appears to lie in the relatively poor access that it gives to the renal pedicle. In operations on tumors of the kidney, hemorrhage is the greatest factor in the mortality. Inability to control bleeding satisfactorily is likely to result from a cramped approach, and in this case Cabot believes that the common use of this incision is an important factor in the still too high mortality in this group of cases. The anterior oblique incision starts relatively farther forward than the classical incision and is continued downward and mesially from a point in about the midaxillary line parallel with the direction of the fibers of the external oblique. It is satisfactory from the point of view of moderate damage to structure and avoidance of the most important nerve trunks. This incision gives relatively poor access to the tumor. It may also damage nervous structures if it is made of thoroughly sufficient length. The nerve-supply of the rectus muscle turns sharply inward and is likely to be divided with the effect of producing more or less paralysis of this structure.

10. Cabot, Hugh: The Operative Approach for Malignant Tumors of the Kidney, *J. Urol.* 14:261-267 (Sept.) 1925.

A third type of incision which Cabot describes is the umbilical: a vertical incision through or at the outer border of the rectus muscle combined with a transverse incision about the level of the umbilicus. This incision gives satisfactory access but is undesirable on account of the inevitable damage to the nerve supply of the rectus muscle. If made of sufficient length to give thoroughly good access, it will be likely to paralyze the greater part of the rectus muscle. The transverse portion of this incision is largely free from objection but its vertical limb is highly damaging. The high transverse incision with cross cutting of the last rib is rarely used, as the vertical portion damages nervous structures. Cabot draws particular attention to a combination of the transverse incision with a vertical incision in the median line. The incision should be started well back in the loin near the anterior border of the erector group. It should be planned to pass not far from the lower border of the twelfth rib, inclining slightly downward until it reaches the median line in the region of the umbilicus. The course of this incision does not traverse any nerve trunks of importance and will not result in paralysis of the rectus or of any important amount of the oblique muscles. It is then met by an incision in the median line carried upward to any necessary extent. This does not damage the nerve supply or other important structure. It allows the raising of a triangular flap which gives direct access to all of the structures of the upper quadrant. Through this incision the costal margin may be lifted as freely as is ordinarily necessary. The peritoneum is lifted from the posterior wall, carrying with it the colon and its mesentery which may be turned inward as far as the median line. This flap of peritoneum with its intestinal and mesenteric content has the effect of keeping the other intestines out of the way and gives a wholly satisfactory view of the field. Cabot believes that this is the least damaging and most satisfactory of all incisions of this type. It is possible to control all the blood supply satisfactorily, especially in the approach to malignant tumors.

Beyer¹¹ states that nephrectomy is the only treatment for renal tumors. Recurrence usually occurs in the scar, more rarely by metastasis. In more than half the cases recurrence appears during the first year after operation. About 15 per cent of the patients may expect a permanent cure; 11 per cent of Beyer's patients were cured. Neither the study of the general or local condition of the patient nor the histologic nature of the tumor can give any definite deduction so far as the prognosis is concerned. Extensive adhesions constitute an unfavorable prognosis. In the discussion of this report, Marion insists on the need

11. Beyer: *Diagnostic et traitement des tumeurs du rein*, Bruxelles méd., 1925, pp. 386-388.

of early diagnosis and cites unilateral hematuria as one of the most important symptoms. He also prefers the lumbar incision with resection of the twelfth rib if necessary. He does not rely on radiotherapy. Chevassu, confirming the foregoing, desires a routine roentgen-ray examination of the chest in order to eliminate pulmonary metastasis, which would be a contraindication to operation. Of ten patients on whom Chevassu performed nephrectomy for renal tumors, one died and several others had recurrences.

Hyman¹² reports a series of seventy cases of renal tumors: forty-four of hypernephroma. Sixty patients were adults and ten were young children under nine years. Fifty were males. More than half of these cases occurred during the fourth and fifth decades. The right kidney was diseased in thirty-eight cases, the left in thirty-two. Calculi were found in three cases. In one of these malignancy was not suspected, a diagnosis of calculus having been established. At operation a suspicious looking area in the cortex was discovered, and on microscopic examination proved to be adenocarcinoma. Hematuria was the first symptom of twenty-one of sixty adult patients. Nine patients had had the initial hematuria within six days whereas the majority had had it weeks, months and even years before. Pain, as an initial symptom, was present in eighteen cases, and not infrequently antedated the appearance of hematuria by many months, and in a few cases, years. Hematuria was the predominating symptom, from a diagnostic point of view as it served to direct the notice of the patient and physician to the urinary tract as the seat of the trouble. The bleeding in some cases was profuse. It may be only microscopic for a long time, before a macroscopic hemorrhage takes place. It is generally painless except where blood clots are passed. Twelve patients (20 per cent) had metastasis when first observed. The points of predilection for secondary deposits are the lungs, long bones, liver and brain. Involvement of the retroperitoneal glands in the region of the kidney was found four times in sixty cases, three times with carcinoma, once with hypernephroma. In children tumors of the kidney have different characteristics from those in adults. The first symptom in many cases is the presence of a large abdominal mass which may sometimes become enormous. The child may appear quite well.

In all cases of renal tumors the one recognizable form of treatment is nephrectomy; radium and deep roentgen-ray treatment are to be used only as adjuvants. Deep roentgen-ray treatment may be of value in inoperable cases for controlling hematuria. In the series of cases in adults there were forty-two in which lumbar nephrectomy and five in

12. Hyman, Abraham: *Clinical and Surgical Aspects of Renal Neoplasms*. Surg. Gynec. Obst. **41**:298-310 (Sept.) 1925.

which transperitoneal nephrectomy were performed, the latter being reserved for very large growths. Besides the usual oblique incision, a transverse lumbar incision has been recommended, dividing, if necessary, one rectus muscle. This incision gives a very good exposure. If a question arises as to the operability of a case, it is advisable to open the peritoneum and examine the liver for metastasis. The renal vein should be ligated as early in the operation as possible to prevent tumor cells from being squeezed into the general circulation. It is important to excise entirely the fatty capsule of the kidney. With transperitoneal nephrectomy there is a higher mortality because peritoneum is opened and there is usually more extensive involvement. In twenty cases the growth had extended into the renal vein; in a few it had extended into the vena cava. This condition does not necessarily make the prognosis more grave. Ten patients in this series with involvement of the renal vein have survived operation for from one to five years. The prognosis in general is bad, death occurring from recurrence, cachexia or metastasis, often as late as ten years after operation. The percentage of three year cures average 20 to 30, and five year cures probably less than 15. The ultimate mortality rate is between 65 and 75 per cent. To reduce this high rate cystoscopy and pyelography should be practiced, not alone in cases of hematuria, but in every case of unexplainable lumbar pain. Patients complaining of intractable sciatica and lumbago should be examined more carefully.

Ed. Note—Hyman's experience with renal tumors is, in general, similar to that reported from the Mayo Clinic, where hematuria as the first symptom was noted in almost 40 per cent of the cases. The appalling feature of this hematuria was that it had been allowed to continue, intermittently, on an average for almost two years before the patient was referred for urologic investigation and surgical treatment. This is, indeed, a grave reflection on our profession as a whole. It is principally by seeing patients early in the disease that we may hope to improve our results in the treatment of renal neoplasms.

In the matter of prognosis we have found the microscopic grouping of these tumors to be a great help, as in cases of malignant cystadenoma. From one to five years after nephrectomy the proportion of living to dead was 2:1; in cases of papillary carcinoma with clear cells (typical so-called hypernephroma) 1:1; in cases of papillary adenocarcinoma with granular cells 1:3; and in cases of alveolar carcinoma 1:7. The greatest single factor in disturbing this ratio was the involvement of the renal vein with tumor tissue in the papillary carcinoma with clear cells. When this occurs the prognosis is generally bad although in all large series of cases exceptions are to be found in which patients with undoubted venous involvement have survived as long as fourteen years.

In our series we had two patients who survived twelve and fourteen years, respectively, and Albrecht¹³ reports the case of one patient who lived twelve years.]

Smith¹⁴ studied sixty-two cases of hypernephroma treated at the Massachusetts General Hospital over a period of twenty-three years. In fifty-two of the cases finally accepted the diagnosis was verified by the pathologist. Thirty-four, or more than half the patients, were between 40 and 60 years, and the patients of from 51 to 60 years were more than twice as numerous as those in any other decade. Forty-three were males, nineteen were females. The right kidney was primarily involved in twenty-seven, the left in twenty-five. In one case both suprarenals contained hypernephromas of approximately equal size. There was hematuria in twenty-seven of the sixty-two cases; in thirty-two none. Pain was noted as being present in thirty-two cases, and absent in twenty-six. The most consistent finding was that of tumor. An enlarged kidney was found in forty-eight cases; in a number of instances the patient himself had noticed the mass. In only one of the twenty-six cases in which nephrectomy was performed was it stated that no tumor was felt. In two other cases no mention of tumor was made. The early occurrence of hematuria is a favorable factor, as it alarms the patient. The value of hematuria as a warning is demonstrated by the fact that in 61 per cent of the twenty-six cases considered suitable for nephrectomy there was hematuria, whereas in only 43 per cent of the entire series was there blood in the urine. Pyelograms were made in ten cases, in all of which malignancy was indicated. The earliest pyelogram was made in 1916; the earliest divided function, by phenolsulphonphthalein, in 1911. There were four operative deaths in the twenty-seven cases; one patient died from embolus during the operation; one, on whom a transperitoneal nephrectomy was performed, died from peritonitis five days after the operation; one died from pneumonia one month after operation, and one from shock a few hours after operation. Eight of the remaining twenty-three patients died within a year, six from extension of the growth, two from unknown cause, possibly from malignancy. Four patients lived three, five, ten and twelve years without signs of recurrence; one patient lived four years, two lived eight years and died from the malignancy. In the entire series results were known to be favorable in nine cases. Of the twenty-seven cases of nephrectomy results were unknown in six. One case, that of a man aged 34, was examined for tumor of the

13. Albrecht, Paul: Beiträge zur Klinik und pathologischen Anatomie der malignen Hypernephrome, *Arch.f. klin. Chir.* 77:1073-1170, 1905.

14. Smith, G. G., and Schoemaker, A. B.: The End-Result of Hypernephroma. *J. Urol.* 14:389-402 (Oct.) 1925.

upper arm, which was amputated. The patient lived for five years. A review of thirty-four inoperable cases showed that ten patients died the first six months after leaving the hospital and a second series of ten died from six to twelve months afterward. Two patients died the following year and three lived from four to seven years. In one case in which necropsy was performed there was hypernephroma of the left kidney and papillary adenoma of the right.

Renal Tuberculosis.—Freudenberg¹⁵ states that tuberculosis of the kidney, usually being unilateral, may affect the mobility of the bladder on the diseased side in such a way as to produce filling defects and distortion of the outlet in the cystogram; this may be of diagnostic value. For instance, the distance of the lateral margin of the bladder from the median line is less on the diseased side. Frequently there is a sharper sloping level in the contour of the diseased side in contrast to the rounded outline on the other. By filling the bladder slowly, while the patient lies absolutely quiet, several exposures may be made. Lagging or failure of the filling out of one side, as the contrast fluid is introduced, may be of significance. This method is thought to be of value usually in cases of late unilateral tuberculosis in which the sensitiveness or small capacity of the bladder makes proper cystoscopic technic difficult. If the ureter in the female is palpable by vagina and the cystogram shows the abnormalities just mentioned, the evidence for tuberculosis on that side is fairly conclusive. With healing of the bladder subsequent to nephrectomy for tuberculosis, there is a corresponding tendency for these roentgenologic findings to approach the normal again in varying degree.

[*ED. NOTE.*—Undoubtedly the study made is of confirmatory diagnostic importance in cases of renal tuberculosis. As Freudenberg points out, the technic of taking the roentgenogram must be carefully executed, as slight changes in the position of the patient, plate or tube may cause an angular irradiation and give a false impression. Probably there are cases, such as the one mentioned by Freudenberg, in which the diagnosis may be safely assumed from such roentgenologic findings. However, it is equally probable that in most instances one could not always attribute the filling defects on one side entirely to tuberculosis. Extravesical growths, intravesical tumor and the like would have to be excluded. Not infrequently, in cases in which the infection of one kidney has progressed to the extent that the corresponding segment of the bladder is extensively diseased, the opposite kidney also is tuberculous. Before operative measures are contemplated, more complete proof is necessary that the lesion is unilateral.]

15. Freudenberg, Albert: Ein röntgenologisches Symptom bei Nierentuberkulose, *Ztschr. f. urol. Chir.* 16:187-193, 1924.

Berard¹⁶ reports the case of a man with a large abscess of the iliac region, which prevented him from walking comfortably and was apparently due to Pott's disease. There had been few symptoms of any kind during the previous year except that from time to time, at the end of micturition, a few drops of pure blood appeared which caused a burning sensation in the urethra. The urine did not contain pus. A mass had appeared a month before admission. It was situated below the antero-superior iliac spine and above Poupart's ligament; it was elongated, fairly hard and painful on pressure. There was no pain on percussion of the spine. The mass extended as high as the lumbar region and could be felt by bimanual palpation. The genital organs were normal and the examination of the urine was negative. The cystoscopic examination was performed with some difficulty; the prostatic urethra was partially obstructed. The vesical neck and interureteral regions were uniformly and intensely red; the ureteral orifices were difficult to find; bleeding occurred constantly; there were no granulations. At operation, Berard, using an oblique costo-iliac incision, found a voluminous irregularly shaped kidney, which accidentally ruptured in one area, freeing caseous pus. Nephrectomy and partial uterectomy were performed. The iliac abscess was incised; it was found to be deep, but could not be connected with any organ and probably was of periureteral origin. Good postoperative results and cure followed, but a small iliac fistula with very little discharge remained. A second cystoscopic examination revealed a large right ureteral orifice, surrounded by an area of congestion, without ulceration or granulation. Berard was in doubt whether he should leave the patient to his general hygienic treatment for tuberculosis or resect the remaining ureteral stump transperitoneally.

Papin¹⁷ reports the case of a young man, belonging to a hemophilic family, exhibiting marked hematuria without any evident vesical or abdominal symptoms or signs. The output of urea was slightly lowered but the urine tests on catheterized specimens were negative, the urine being perfectly clear between spells of hematuria. Papin was compelled to perform nephrectomy on account of the excessive hemorrhage. A large bluish red kidney, containing a few fine granulations but surrounded by a perfectly normal capsule, was extirpated. The surgical-pathologic diagnosis was tuberculosis. A small vessel had been eroded and almost occluded by a thin coat of fibrin. This may have been the source of hematuria, along with the hemophilic constitution of the patient. Death took place suddenly following embolism.

16. Berard: Sur une forme assez rare de la tuberculose génito-urinaire: Gros rein droit caséux fermé: Volumineux foyer de périurétérite suppurée, simulant un abcès froid pottique au-dessus de l'arcade de fallope, *Lyon chir.* 21:769-771, 1924.

17. Papin, Marc: Tuberculose rénale unilatérale à symptomatologie uniquement hémorragique chez un hémophile, *J. d'urol. méd. et chir.* 20:69-72, 1925.

Blanc¹⁸ examined a young woman with advanced tuberculosis of the left kidney. The cystoscopic examination revealed a double ureteral orifice on the right side. The urine from one of the halves of the right kidney also indicated tuberculosis. Pyelograms taken with two different catheters revealed that the superior pelvis corresponded to the superior orifice in the bladder and the inferior pelvis to the inferior orifice. The superior half had a small pelvis and appeared to be atrophic; the inferior one, larger in size, was thought to be tuberculous. The phenolsulphonphthalein return was good from both renal segments. Left nephrectomy was performed. The upper right atrophic kidney as well as the infected lower one compensated very well, and three months after operation the phenolsulphonphthalein return was 60 per cent. Blanc stated that in cases of double ureter one should always determine which kidney corresponds to each ureteral orifice by a pyelogram taken with two catheters. The functional value of a kidney does not always correspond to the amount of parenchymatous tissue, and a small pelvis does not necessarily indicate an atrophic kidney. A small apparently atrophic kidney may be capable of an unexpected hyperfunction. When a renal mass is composed of two separate unequal segments, the smaller superior portion does not always correspond to the diseased area. A slightly infected tuberculous kidney may show considerable compensatory hypertrophy after the removal of the more seriously infected opposite kidney. With the aid of the phenolsulphonphthalein functional test, one may follow step by step the development of the functional activity of a kidney and its progressive hypertrophy.

[ED. NOTE.—This case is interesting in that the relationship between the ureteral orifices and the renal segments is opposite to that usually found in cases of double kidney. When two ureteral buds are present, as the result of changes in the position of the duct and the rotation and ascent of the two renal segments, it generally develops that the lower ureteral orifice drains the upper kidney. Papin reported a case of bilateral tuberculosis in which the left kidney was partially resected; later right nephrectomy was performed. No report on the later results of Papin's case was obtainable. It would also be interesting to know the late results in Blanc's case. Braasch has shown that improvement is generally noted in other tuberculous foci after the removal of a tuberculous kidney. This is more marked when there is a focus in the lungs or joints. Hinman has shown that in the case of partially destroyed kidneys the return of function in the remaining kidney is at times prompt after excision of the opposite kidney.]

18. Blanc, H.: A propos d'une tuberculose rénale gauche avec duplicité complète de l'uretère du rein droit, *J. d'urol. méd. et chir.* 20:47-57, 1925.

Persson¹⁹ presents a clinical study of renal tuberculosis at the surgical clinics of the Seraphimer Hospital, Stockholm, during the period from 1890 to 1920. There were 295 patients; 194 (65.8 per cent) were men, and 101 (34.2 per cent) were women. Operation was performed in 205 cases and in ninety it was not. In five cases the disease occurred in the first ten years of life, in four cases the age was more than 60, and in 227 cases it was between 30 and 60. Symptoms of other tuberculous lesions occurred in about half the cases as follows: pulmonary tuberculosis, sixty-six cases (22.4 per cent); genital tuberculosis (male), forty-six cases (15.6 per cent); tuberculosis of bones and joints, twenty-one cases (7.1 per cent); pleuritis,

TABLE 1.—*Operative Mortality and Relation of Mortality to Age of Patients in One Hundred and Ninety Cases of Nephrectomy for Unilateral Tuberculosis*

| | |
|--|------------|
| Patients who died from six to eighteen years after operation..16 | |
| Operations for unilateral renal tuberculosis..... | 190 |
| Operative mortality | 14 (7.3%) |
| Patients with complete postoperative data..... | 182 |
| Patients who died after dismissal from the hospital..... | 45 (24.7%) |
| Patients who died within three years after operation..... | 21 |
| Patients who died more than three years after operation..... | 24 |
| Patients who died from one to five years after operation..... | 29 |
| Patients who died from six to eighteen years after operation.. | 16 |
| KNOWN CAUSES OF DEATH IN FORTY-FIVE CASES | |
| Patients who died within four years..... | 24 |
| From disease of remaining kidney..... | 12 |
| From pulmonary tuberculosis..... | 7 |
| From miliary tuberculosis..... | 5 |
| Patients who died more than four years after operation..... | 21 |
| From disease in remaining kidney..... | 9 |
| From pulmonary tuberculosis..... | 9 |
| From miliary tuberculosis..... | 1 |
| From spondylitis with paraplegia..... | 1 |
| From peritoneal tuberculosis..... | 1 |

seven cases, and lymphadenitis, ten cases. There were eighty-four cases without operation in which the later results of the disease were known. Death occurred in seventy-one (84.5 per cent). Two years after onset of the disease death occurred in twenty-six (31 per cent); from three to five years after, in twenty-seven (32 per cent); from six to ten years after, in twelve (14.3 per cent), and more than ten years after, in six (7 per cent). Renal and urogenital tuberculosis and its sequels, general cachexia and uremia, are in great preponderance, forming about 80 per cent of the causes of death.

The operative mortality in 190 cases of nephrectomy for unilateral tuberculosis and the relation of mortality to the age of the patients are shown in table 1.

19. Persson, Mauritz: Renal Tuberculosis: A Clinical Survey of 295 Cases. Ninety of Which Were Not Operated On, *Am. Surg.* 82:526-551 (Oct.) 1925.

Persson considers those patients as well who, three years or more after operation, have been found free from a troublesome desire to urinate, smarting pains on urination, considerable pyuria and hematuria, and who have, besides, almost totally regained their strength and power to work, and, finally, have increased in weight. In 104 cases these requirements were fulfilled so that definite cure occurred in 57.1 per cent. The observation period was from twenty-three to twenty-five years in two cases, from fifteen to twenty years in eleven cases, from ten to fourteen years in twenty-six cases, from five to nine years in thirty-nine cases, four years in sixteen cases, and three years in ten cases.

A detailed discussion of the method of wound closure is given. The best results were obtained by primary suture. In sixty-two of sixty-four cases in which the ureter was ligated and dropped into the wound and primary suture carried out, the wound was healed in a period of two weeks. Whenever any infection of the wound occurred the wound was drained usually for only three or four days. Complete data on 135 cases of wound healing is given. Of the sixty-two women who were of an age for conception, ten gave birth after operation to a total number of seventeen children. Of these nine gave birth to a total of fourteen normal children and to one fully developed, stillborn child. In the last instance, nephrectomy and, four months later, secondary ureterectomy, had been carried out during pregnancy. These nine women are now healthy and have no trace of albuminuria.

Renal Function.—Levy and Falci,²⁰ after an analysis of eight cases of renal tuberculosis (in four of which operation had been performed), came to the following conclusion: In bilateral renal tuberculosis, the concentration and output of urea and chlorides, worked out separately for each kidney, do not give satisfactory evidence of the function of the investigated kidney. A high percentage of urea in the blood and marked polyuria also may lead to erroneous conclusions and cause fatal mistakes. On the contrary, the study of phenolsulphonphthalein elimination gives an accurate estimation of the condition of the kidney: it should be resorted to each time intervention is considered. If the output of phenolsulphonphthalein in the least damaged kidney does not indicate a serious effort at functional compensation, operation should be avoided by all means. In principle, nephrectomy should never be attempted in a case of bilateral disease if the remaining kidney does not excrete more than 50 per cent of the phenolsulphonphthalein in seventy minutes.

20. Levy, R., and Falci, E.: Les indications de l'épreuve de la P. S. P. dans le traitement de sa tuberculoses rénales bilatérales. *J. d'uroł. méd. et chir.* 19:13-22, 1925.

[ED. NOTE.—For many years the various correlated concentrations of salts in the blood and urine have served as an index of renal sufficiency. Many articles on the urea concentration index have appeared in French medical literature. It is of interest to note that dye excretion functional tests are becoming more popular with French urologists.]

Shaw,²¹ after an extensive investigation of the elimination of phenolsulphonphthalein in normal and abnormal conditions, was able to find a definite normal curve and significant variations from this in several diseases. The normal curve of its elimination was determined by a series of forty-four tests on twenty-three normal persons in which the urine was collected at fifteen-minute intervals for two hours. The curve was characterized by an average output of 40 per cent during the first fifteen-minute period, 17 per cent during the second, 8 per cent during the third, 4 per cent during the fourth, and a gradual decrease to 0.5 per cent during the eighth fifteen-minute period.

There were one or more tests performed in the same manner in fifty-six known cases of renal disease. In all of these cases, in which renal insufficiency was demonstrated by any other tests, there were definite abnormalities in the curve and in several cases the presence of an abnormal curve indicated impending renal failure, while the other tests were negative.

A majority of the cases studied were those of renal damage from back pressure and infection. In this group a striking feature was an increase in appearance time and a delay in the peak of elimination. In the cases followed with repeated tests, the peak of elimination occurred earlier as the kidneys improved while the two hour output often remained unchanged.

The number of cases of nephritis and vascular disease of the kidney studied have been too few to justify conclusions, but the results obtained indicate that by more frequent collection of the specimens more information may be gained from the phenolsulphonphthalein test and that renal impairment may be demonstrated even when undetectable by the test as usually performed.

In most of the cases quoted, the two hour output was quite normal and in many the output in the first hour would be considered normal, yet definite variations in the fifteen minute curve were noted.

It is realized that the collection of urine specimens at fifteen minute intervals is not necessary as a routine, but in cases in which exact information concerning the kidney's ability to eliminate phenolsulphonphthalein is desirable, such a modification of the test may be useful.

21. Shaw, E. C.: A Study of the Curve of Elimination of Phenolsulphonphthalein by the Normal and Diseased Kidneys, *J. Urol.* **13**:575-591 (June) 1925.

Although some of the finer points of the test are lost when collections are made at intervals exceeding fifteen minutes, for routine, thirty minute collections are practicable and give much more information than the hourly collections that are usually made. The authors think it important to date the collection from the time of administration of the phenolsulphonphthalein rather than from the time of appearance of the drug in the urine. In this way the appearance time, which is often of great importance, is incorporated in the percentage figures rather than existing as a separate entity. Examination of the abnormal curves show the advantages of this arrangement.

[ED. NOTE.—This report is most encouraging. Urologists who use the phenolsulphonphthalein test as a routine, frequently find that the results of this test do not correspond to the blood nitrogen studies. Yet simplicity makes the phenolsulphonphthalein test a desirable one for routine. With Clay's modifications in technic, some of the disadvantages of the test may be eliminated.]

Negro and Colombet,²² after studying the nonparallel excretion of urea and phenolsulphonphthalein (what they term "*le désaccord ureophthaleinique*") of polycystic kidneys in several cases, conclude: (1) The elimination of urea in cases of polycystic kidney may be satisfactory in amount but its concentration never reaches a normal level (this is due to marked polyuria which accompanies this disease); (2) if the phenolsulphonphthalein is not eliminated in the same proportions as the urea, it is because the phenolsulphonphthalein, being independent of the polyuria, cannot pass in greater proportion than is compatible with the real excretory power of the kidney. The result is the "*désaccord ureo-phthaleinique*" and it shows also how the phenolsulphonphthalein alone indicates the exact value of the kidney. In one case this disaccord was not present; the urea retention was high (1.07 per cent) and the phenolsulphonphthalein was low, but the urinary output was poor and the patient died in uremic coma. This case, which corroborates the previous conclusions, led the authors to advance the following hypothesis: During the long period of evolution of the cysts, polyuria provokes a marked output of urea which compensates more or less for the mediocre renal power of concentration. Uremic troubles take place later while cystic degeneration progresses along with gradually diminishing diuresis. This disaccord is very marked during the period of polyuria; it then tends to disappear while diuresis diminishes. Lower excretion of urea and phenolsulphonphthalein reach a parallel level when the polyuria has ceased; their degree of excretion then remains parallel following a more and more decreasing curve until death takes place.

22. Negro, Mario; and Colombet, G.: *Considérations nouvelles sur le fonctionnement du rein polykystique*, J. d'urol. méd. et chir. 20:20-26, 1925.

Rabinowitch²³ reports a study of the results in cases in which the diazocolor reaction for uremia was used. The technic of the first part of the test is identical with the van den Bergh bilirubin reaction (indirect method) except that the blood may be oxalated. To 1 cc. of plasma or serum is added 2 cc. of 96 per cent alcohol solution. The proteins are allowed to precipitate and the mixture is filtered or centrifugalized. The clear filtrate or supernatant fluid from the centrifuge specimen is collected. To 1 cc. of this clear fluid is added 0.5 cc. of alcohol and 0.25 cc. of diazoreagent freshly prepared. The mixture is then boiled for thirty seconds and then a few drops of 10 per cent solution of sodium hydroxide is added. The characteristic reaction is the very rapid development of a pink color which also disappears rapidly. The data obtained in this study showed that the reaction is positive only in cases of marked retention of nitrogen associated with definite lesions, such as advanced nephritis or acute surgical diseases of the kidney and pyelonephritis. In cases of albuminuria, hypertension, even with retinal changes and definite impairment of concentrating power, the test is negative. A negative reaction is also seen in patients with nitrogen retention due to mechanical obstruction and subsequent renal insufficiency when actual renal damage is not great. One case is cited. The patient suffered from bilateral renal tuberculosis with anuria three days before admission when the blood urea nitrogen was 90 mg. and creatinine 6 mg. for each 100 cc. The reaction was negative. A month later the blood urea nitrogen was 96 mg. and the reaction still negative. Later nephrectomy was followed by marked improvement. Then, as the urea nitrogen began to rise again, the test became positive and soon the patient became uremic and died. This is interpreted as showing at first an obstructive nitrogen retention, but as the destruction of renal tissue became more marked the reaction became positive.

[ED. NOTE.—This test should be of use in distinguishing between actual renal damage and transitory damage due to back pressure in our cases of prostatic obstruction. In this way a prognosis might be quickly arrived at in some cases.]

Renaud²⁴ stated that nephritis in patients with cancer had usually been ascribed to intoxication by neoplastic cells. In studying the renal function in different stages of the disease, Renaud was able to make out that the nephritis was one of the most important factors causing death in cases of cancer. He also found that nephritis was not directly dependent on the neoplasm and had often the character of an accidental complication. From an anatomic standpoint kidneys of patients with

23. Rabinowitch, I. M.: Observations on the Value of the Diazocolor Reaction in the Differential Diagnosis of Uremia, *Canad. M. A. J.* **15**:725-728 (July) 1925.

24. Renaud, Maurice: Les reins et les fonctions rénales des cancéreux, *Bull. de l'Assn. franç. p. l'étude du cancer* **13**:632-657, 1924.

cancer may be classified: (1) kidneys without lesions; (2) kidneys without chronic lesions, but exhibiting lesions of toxic infectious nephritis, or with pyelonephritis by ascending infection, and (3) all the preceding kidney diseases, but superimposed on a chronic nephritis the origin of which antedated the neoplasia. In principle, patients with cancer usually have one kidney which functions perfectly normally. The nephritis can be considered as a complication of cancer. The comparison of the results given by the anatomic and the clinical study of this type of nephritis are not always in accordance; almost all post-mortem examinations of kidneys show some type of lesion in cases of cancer; on the other hand, during the evolution of the cancer, the exploration of renal function shows almost no renal insufficiency and almost no symptoms of nephritis.

URETER

Surgical Technic.—Marion,²⁵ in a discussion of ureteral suture at the meeting of the Société de chirurgie of Paris, reports the case of a patient operated on by Petit. The right ureter was severed during removal of the uterus. The ureter was sutured end-to-end over a catheter which was left in place seven days. One month after operation, regular ureteral catheterization was instituted and continued over a period of twelve months, both to verify the permeability of the ureter and to maintain its caliber. The involved kidney remained normal and twenty months later its function was normal, and a no. 12 catheter could be inserted into the ureter. Marion states that such results are unusual. In most cases, suture of the ureter causes stenosis, distention of the kidney and later necessitates nephrectomy. A discussion on ligation and suture of the ureter in similar cases followed Marion's remarks. J. L. Faure stated that ureterocystostomy is a doubtful operation. He believes in performing nephrectomy, unless the condition of the opposite kidney is not known. Tuffier recalled the method of Israel who ligates the severed ureter which causes atrophy of the corresponding kidney. Lecené believes that this procedure is dangerous, because the ligature usually is made in septic tissues, and ascending infection, necessitating an emergency nephrectomy, may readily occur.

McArthur²⁶ reports the repair of a constricted ureter, the delayed result of trauma. It had been operated on previously and the kidney drained. The former renal incision was reopened and the kidney was

25. Marion: Section accidentelle de l'uretère au cours d'une hystérectomie pour gros fibrome inclus dans le ligament large droit; suture bout à bout sur une sonde urétérale; drainage abdominal, résultat vingt mois après, Bull. et mém. Soc. nat. de chir. 51:910-919, 1925.

26. McArthur, L. L.: A New and Simple Repair of Ruptured or Strictured Ureters, Surg. Gynec. Obst. 41:719-721 (Dec.) 1925.

found rigidly fixed by the excessive infiltration and the fatty capsule was fibrotic. McArthur describes the technic of his operation: Given a missing portion of a ureter, even 2.5 or 5 cm. in length, a longitudinal slit is made in the side of the proximal portion sufficiently long to admit two catheters. One of these, a rubber urethral catheter, is inserted upward to the renal pelvis; the second, a ureteral catheter of good size, is inserted downward so that it passes out of the proximal fragment, and bridges the gap to the proximal end of the distal fragment. Both ends of the ureters are then approximated as closely as feasible by absorbable sutures. The catheters are then brought to the surface and permanently secured to the skin by stitches or other devices. All the urine from that kidney is thus diverted from the field of operation during the time of epithelization. The body tissues heal together around the catheter, bridging the gap between the renal and the vesical ends, and the catheter simply remains in place until in the judgment of the operator an epithelial lining has had time to grow between the ends. The catheters in McArthur's case were removed nine weeks after operation. There was no further escape of urine. The wound immediately healed and the quantity of vesical urine doubled at once. Two years later the patient was perfectly healthy.

Ureteral Stones.—Sacchi²⁷ says that ureteral stones may remain unnoticed for a long time although their presence gives rise to continuous trouble. He follows Marion's principle and makes a roentgenogram in every case of pyuria which is not definitely proved to be tuberculous. If this is not conclusive, an opaque catheter should be passed, and if this is unsatisfactory, a pyelogram is taken. In one of Sacchi's cases four shadows, apparently of stones in the pelvis a little to the right of the median line, did not correspond to the course of the ureter. The opaque catheter, which passed without encountering any resistance, was seen 1 cm. from the shadows. A ureterogram revealed the connection between ureter and stones which proved to be embedded in a true ureteral pouch of a markedly dilated ureter.

Lower²⁸ believes that the simplest and easiest avenue of approach to ureteral stone within the pelvis in the female is through the vagina. This is particularly the case when the stone can be palpated through the vagina.

The technic is simple. With the patient in the lithotomy position, the cervix is caught with a curved tenaculum and pulled well to the opposite side, thus pulling down the base of the bladder and the ureter. The stone is palpated and an incision made through the mucous mem-

27. Sacchi: *Considérations a propos de quatre cas de calculs de l'uretère*, J. d'Urol. méd. et chir. 20:27-40, 1925.

28. Lower, W. E.: *Removal of Stone from Lower Ureter by Vaginal Route*, J. Urol. 14:113-117 (Aug.) 1925.

brane of the vagina parallel to the ureter. The tip of the index finger is then pushed through this slit and the ureter and stone are located. A tenaculum is then placed above the stone to prevent it from moving up the ureter. By releasing the traction on the cervix and by gentle traction of the tenaculum on the ureter, the ureter and stone are brought within the opening in the vaginal mucous membrane, at which point the stone can readily be removed through a longitudinal opening. The incision in the ureter is closed with a few fine, absorbable sutures and the ureter is released. A small cigaret drain is inserted through the vaginal slit and is removed at the end of the second day. If there is no leakage of urine, and there is not likely to be, the patient can usually leave the hospital three or four days after the operation. This method affords dependent drainage, avoids external incision and shortens the period of convalescence.

Francois,²⁹ in three cases of calculus of the inferior extremity of the ureter in which an injection of a proprietary form of oil of cajuput above the stone and electrocoagulation of the ureteral meatus did not cause the stone to pass, removed the stone surgically; a low extraperitoneal incision was made in order to reach the ureter. Cure followed in all cases. François follows several procedures in obtaining his diagnosis of impacted ureteral calculus; first, a simple roentgenogram is taken which may reveal a shadow in the bony pelvis; second, an opaque catheter is introduced into the ureter and two roentgenograms are taken at different angles. If the suspected shadow touches the opaque sound in both pictures, one may be reasonably certain of the presence of a ureteral stone. The graduated opaque catheter (a catheter with portions opaque to roentgen rays alternating with nonopaque segments) will determine the exact site of the calculus in connection with the ureteral orifice. If the stone lies less than 1 cm. from the ureteral meatus, one may hope to have it pass to the bladder by making a slit in the ureteral meatus with electrocoagulation. If this method fails or if the calculus is higher, one must not wait too long before operation for fear of hydropyonephrosis.

[ED. NOTE.—Urologists in this country use the ureterogram more frequently than the shadowgraph catheter in forming a diagnosis of ureteral stone. The nodular disposition of the opaque medium around the stone, the distention of the ureter above the obstruction and in some cases an absence of the medium above the shadow, while present directly below it, are the main points to consider in the diagnosis. A positive ureterogram together with obstruction to the catheter is usually sufficient to make a definite diagnosis.]

29. François: Trois cas de calculs de l'extrémité inférieure de l'uretère, enlevé par la voie parapéritonéale, Bruxelles méd. 5:1413, 1925.

Chute³⁰ states that infection of the abdominal lymph nodes, which is usually tuberculous, occurs quite commonly, not only in children but also in young adults; it is occasionally seen even in older persons. The condition is subacute, as a rule, and causes vague abdominal discomfort rather than pain; however, it may at times be absolutely painless. Sometimes the pain is acute enough to lead to the removal of the appendix or to abdominal exploration. The condition is generally of less interest to the urologist than to the general surgeon. In the process of cure of these inflamed lymph nodes, calcification often takes place, as is the case in the cure of tuberculous lymph nodes elsewhere. These calcified abdominal nodes are of considerable interest to the surgeon since in their roentgenographic appearance they are easily mistaken for urinary calculi. This simulation may be very close indeed and must be constantly borne in mind in considering the nature of any shadows that have been found in patients suffering from symptoms that might be due to renal stones; the question of calcified abdominal lymph nodes need not be considered when branched coral-like shadows are seen. In carrying out roentgenographic investigation in cases in which the symptoms suggest the possibility of renal or ureteral stones, shadows are often thrown by calcified abdominal lymph nodes. These shadows can usually be easily distinguished from those of urinary stones by their mottled appearance and mobility. Occasionally the roentgenographic catheter, with or without stereoscopic plates, will be necessary to determine whether a given opaque body is in a ureter or not. Rarely a pyelogram may be necessary to determine whether a given shadow is of renal or extrarenal origin.

Marion³¹ reports three cases in order to emphasize the importance of catheterizing the ureters in cases in which renal stones are being passed; relief from pain and even cure may be obtained by this procedure. The first case was that of a woman who, for three weeks, had suffered from almost constant pain in the right ureteropelvic region, eased only by morphine. The passage of the catheter relieved the patient instantaneously. The catheter was left in place for a few days and the stone was removed later without incident. In the second case a differential diagnosis between renal and hepatic colic was almost impossible. In order to help the diagnosis as well as the pain, a catheter was passed into the ureter; 17 cm. deep it struck something hard which it finally passed; a stream of urine was liberated. Pain which had been constant and severe for twenty-five days vanished immediately and

30. Chute, A. L.: *The Difficulty in Distinguishing Between the Radiographic Appearance of Urinary Stones and Calcified Abdominal Glands*, *J. Urol.* **14**:489-500 (Nov.) 1925.

31. Marion, G.: *De l'utilité du catheterisme ureteral dans la colique nephritique par lithiase*, *Presse méd.* **33**:1043 (Aug. 5) 1925.

with the cystoscope; it will consist of destruction of the mass and "meatotomy" if the ureteral orifice is constricted.

Ureteral Transplantation.—Marion³³ states that ureteral transplantation is of doubtful value. If a transplantation is performed, one should always be ready to operate on the corresponding kidney in case of complications. He suggests that in some cases, instead of reimplantation primary or secondary nephrectomy may be more desirable. He believes that, in most cases, the kidney of which the ureter has been transplanted becomes dilated and gradually atrophies. Sometimes patients do not notice the disappearance; in other cases the immediate result is good, but later complications arise which necessitate nephrectomy; finally, in other cases, the immediate result is bad and compromises the result of the primary intervention. In a period of from fifteen days to two months three of Marion's patients died. He attributed the deaths to accidents of pyonephrosis developed as the result of transplantation of the ureter. Legueu, taking part in the discussion, confirmed Marion's statements. He found only one favorable case in the literature, that of a patient who, seventeen years after transplantation of the ureter, still had a well functioning kidney.

[ED. NOTE.—In transplanting the ureter for various operations on the bladder the possible preservation of renal tissue is not sufficiently important to justify the further expenditure of time during the operation. In many cases the ureter in question has already become obstructed and the corresponding kidney greatly reduced in function. Hunt³⁴ reported ninety-eight cases of segmental resection of the bladder with ligation and transplantation of the ureter for malignant tumors. In forty-five cases the ureter was disposed of by ligation, with six post-operative deaths, a mortality rate of 13.3 per cent. Necropsy disclosed acute pyelonephritis in all cases. Nephrectomy as a result of infection superimposed on hydronephrosis was necessary in two cases, one five days after operation followed by death, the other thirty days after operation with recovery. In fifty-three cases the ureter was disposed of by transplantation with sixteen deaths, a mortality rate of 30.1 per cent. Death occurred from the third to the fifty-third day. The clinical cause of death in each instance was ascending infection. Subsequent nephrectomy was resorted to in only one case, nine years after the first operation.

In those cases in which it is necessary to consider transplanting the ureter it may usually be inferred that the malignant disease is extensive,

33. Marion: Discussion sur les implantations ureterales, *J. d'urol. méd. et chir.* 20:58-59, 1925.

34. Hunt, V. C.: Disposal of the Ureter in Surgical Excision of Malignant Tumors of the Bladder, *J. Urol.* 14:19-31 (July) 1925.

and often infection is present in the surrounding tissue as well as the kidney. The high death rate is a result of the severity of the condition more than of the operative procedure. It is likely that something may be accomplished in the future in certain of these cases of extensive vesical carcinoma by total cystectomy and transplantation of the ureter into the colon.]

Papin³⁵ discussed the exclusion of the urinary bladder. Deviation of urine from the bladder may be obtained either by nephrostomy or by transplantation of the ureter to the skin or to a hollow organ. Nephrostomy is unsatisfactory; it is a bloody operation, causes lesions of the renal parenchyma, necessitates drainage against gravity, and the collecting apparatus is usually fixed so that the patient cannot directly control it. Ureteral transplantation is more satisfactory. Papin gives the following facts about this procedure:

1. An isolated ureter does not become necrotic if it is not separated from its connective sheath.

2. Isolation of the ureter from its normal connections disturbs its functioning power; it becomes atonic and dilated and contracts more slowly and less frequently.

3. It is impossible to avoid the atonic dilatation of the ureter, but this develops slowly. Dilatation by stricture or kinking, which is rapidly progressive, can be avoided by correct surgical procedures.

4. All surgical procedures cause infection; the resulting dilatation of the ureter is responsible for most infections.

Papin gives three methods of transplanting the ureter. Transplantation to the skin, which is a relatively safe operation, may be carried out in the hypogastric region, in both flanks, in the lumbar region or preferably in the iliac region. One of the author's patients is still doing well after iliac ureterostomy performed five years ago. The second method, transplantation of the ureter into the urethra, is dangerous and should not be done. The third method, transplantation to the intestine, is occasionally performed but Papin considers it a dangerous operation; it causes peritonitis, acute pyelonephritis, anuria, and the mortality is high. The Mayo Clinic reports a satisfactory series of cases of transplants to the intestine; only one death occurred in thirty-five cases. This success is due to the fact that the operations were performed in two stages. In a series of operations by Russian surgeons there were sixty-one deaths in ninety-eight cases. Papin reports the following series of compiled reports: In cases of total cystectomy the mortality of transplantation to the skin was 28 per cent; to the intestine, 59.2 per cent; to the vagina, 50 per cent; to the urethra, 100 per cent (eight cases). Death occurred in ten of eighteen cases of

35. Papin, M.: La dérivation haute des urines, *Presse méd.* **33**:1412-1413, 1925.

inoperable tumor of the bladder following transplantation of the ureter into the bowel; for the same condition death occurred in one of five cases of double nephrostomy and in seven of twenty-two cases of double ureterostomy.

Ureteral Stricture.—Kretschmer³⁶ reports four cases of so-called congenital stricture of the ureter. The etiology of this condition is obscure. The first case was that of a child aged 7 months. At operation a large hydronephrotic kidney was found with a stricture of the ureter about 1 cm. below the renal pelvis. Nephrotomy, not nephrectomy, was performed, because there was no proof of the presence of a normal kidney on the opposite side. After the operation all urine came through the renal wound. The patient died two weeks later. Necropsy showed bilateral hydronephrosis and bilateral stricture of the ureter. The second case was that of a male child aged 5. At cystoscopy a prompt flow of very turbid urine was obtained from the left kidney. The urine from the right kidney was clear. A pyelogram showed enormous dilatation of the right kidney. At operation a stricture of the ureter at the ureteropelvic junction was found. This patient recovered uneventfully. The third case was that of a male child aged 3. The diagnosis of stricture of the ureter with hydro-ureter, hydronephrosis and superimposed infection was made. The fourth case was that of a female child aged 7 months. A pyelogram revealed enlargement of the right renal pelvis. Bottomley reports twenty-five cases occurring in children under the age of 5; in five the stricture was bilateral. Kretschmer draws attention to the discrepancy that may exist between the urinary findings and the condition present in the kidneys, and between the symptoms and the site of disease, especially in acute cases, which makes a definite diagnosis of ureteral stricture at times very difficult before operation.

36. Kretschmer, H. L.: Congenital Stricture of the Ureter, Surg. Gynec. Obst. 41:713-719 (Dec.) 1925.

(To be Continued)

THE CONTROL OF INTRACTABLE PAIN IN LUMBAR REGION, PELVIS AND LOWER EXTREMITIES

BY SECTION OF THE ANTEROLATERAL COLUMNS OF THE
SPINAL CORD (CHORDOTOMY)*

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The intense, intractable pain associated with primary or metastatic growths in the spine has always elicited the sympathy of the medical profession, but our efforts to afford adequate relief have in general been unsatisfactory. Almost as futile have been our attempts to alleviate the pain of inoperable uterine carcinoma with extensive pelvic metastases and of advanced malignant disease in the lower extremities. This pain, while sometimes not as severe as that associated with spinal cord lesions, is still accountable for an untold amount of suffering.

The routine administration of morphine in ever increasing doses and at shorter intervals has been almost universally accepted as the only palliative means at our disposal. Those of us, however, who have seen these patients linger on week after week and even month after month, begging for something to relieve their suffering, have felt at times as though almost any means is justifiable. Unfortunately morphine, while so efficacious in most diseases, has here proved unsatisfactory; a dose sufficient to benumb the mentality is required to control the pain. A tolerance for the drug is quickly acquired and as the disease may continue for months, enormous doses are ultimately needed to afford even partial relief.

It is for this reason that numerous surgical procedures for the abolition of pain have from time to time been suggested. The operation that has been most frequently applied is that of rhizotomy. Dana first proposed division of the posterior roots for the relief of severe neuritic pains, and following his suggestion Bennett in 1886 and Abbe in 1888 divided certain posterior nerve roots. In 1908 Förster recommended rhizotomy for the relief of gastric crisis. Since that time a rather large number of patients have been operated on with varying degrees of relief. On the whole the operation has fallen into ill repute.

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Theoretically, rhizotomy should give perfect relief but practically the results have been disappointing. Many of the operations undoubtedly failed because an insufficient number of nerve roots were cut. This explanation, however, is not always applicable. Elsberg¹ says:

I have never seen a good result when the operation was performed for the pain of metastatic malignant disease or arthritis of the vertebrae, no matter how large the number of roots divided.

He points out that while nerve root neuralgias, as from direct bony or inflammatory pressure, can with almost complete certainty be cured by rhizotomy, pain from peripheral lesions may be unchanged and suggests that the wide anastomosis of peripheral nerves may account for the failures in the latter group. Frazier² has had much the same experience. He says:

Unfortunately, the results of posterior root section for the relief of intractable pain have not fulfilled the expectations of the inceptors of the operation; and while chronologically pain is the primary indication for rhizotomy, this operation has been found to be much more effective in the treatment of spasticity and visceral crises, to which it was later extended.

Not only does rhizotomy frequently fail to afford relief, but there are at least two serious disadvantages to the operation. Because of the wide overlapping of the sensory nerves it is imperative that at least three consecutive roots be divided to obtain anesthesia in even a small area. It is therefore evident that at least two roots both above and below the particular segments that we wish to anesthetize must be sectioned. In malignant growths the area of pain is usually large, requiring an extensive laminectomy, frequently in these weakened patients a hazardous procedure.

The second objection to rhizotomy is the complete anesthesia that inevitably accompanies the complete analgesia. Loss of pain and temperature sense in no way seriously inconveniences the patient, but the additional loss of sensations of touch, motion and position is a definite handicap. To overcome this complication every third root may be left intact. While this will insure some touch sensation it unfortunately will not completely abolish pain. Partial or complete paraplegia and incontinence of urine have been described as occasional complications of root section. Other operations on the posterior roots, their ganglions, or on the peripheral nerves have proved even less satisfactory.

1. Elsberg, C. A.: *Diagnosis and Treatment of Surgical Diseases of the Spinal Cord and Its Membranes*, Philadelphia, W. B. Saunders Company, 1916, p. 153.

2. Frazier, C. H.: *Surgery of the Spine and Spinal Cord*, New York, D. Appleton & Co., 1918, p. 629.

A still more radical procedure to relieve the excruciating pain associated with malignant spinal metastases was proposed by Cushing.³ In 1910 he suggested "the deliberate transection, either of the entire cord or of the posterior columns alone, cephalad to the lesion," and in 1916 performed such an operation.⁴ The patient was a woman suffering from spinal metastases with a paralysis below the twelfth thoracic segment. He divided the cord in the thoracic region, well above the lesion, with an entirely satisfactory result, the patient being practically free from pain until the time of her death six months later. Such a radical operation would, of course, only be justifiable when the motor function was already lost, but the operation has been seriously proposed in a number of cases.

Knowing the drawbacks and uncertainties of the previously advocated procedures for the relief of intractable pain, we studied with growing interest Frazier's first series of chordotomies, based as they were on an exact knowledge of spinal cord topography. This operation was made feasible by the work of several men, particularly Spiller, who by clinical observations and experimental investigations laid the basis for our present knowledge of spinal pathways.

Van Gehuchten in 1893 first expressed the definite opinion that the fibers conveying pain and temperature sensations passed up the cord in Gowers' tract, although Gowers had suggested this in 1879. Others supported his views, but no actual proof was afforded until Spiller's⁵ fortunate observation of a patient at the Philadelphia General Hospital in August, 1904. This man had practically complete loss of sensation for pain and temperature in the lower limbs with preservation of tactile sensibility. He was under observation for some months and died in January, 1905. The necropsy revealed a solitary tubercle involving the right Gowers' tract at the extreme lower end of the thoracic cord and slightly above this a second solitary tubercle implicating the left tract of Gowers.

This absolute localization of the pain fibers and the evidence that no important motor or tactile sensory fibers passed in this tract led Spiller in 1911 definitely to propose section of the anterolateral column for intractable pain. It had previously been suggested by Schüller (1910) as a substitute for section of the posterior roots in cases of

3. Cushing, Harvey: *The Special Field of Neurological Surgery: Five Years Later*, *Bull. Johns Hopkins Hosp.* **21**:325 (Nov.) 1910.

4. Cushing, Harvey: *The Special Field of Neurological Surgery After Another Interval*, *Arch. Neurol. & Psychiat.* **4**:603 (Dec.) 1920.

5. Spiller, W. G.: *The Occasional Clinical Resemblance Between Caries of the Vertebrae and Lumbothoracic Syringomyelia, and the Location Within the Spinal Cord of the Fibers for the Sensations of Pain and Temperature*, *Univ. Penn. M. Bull.* **18**:147 (July-Aug.) 1905.

gastric crisis. Later observations have convinced Spiller that the fibers of pain and temperature sensation lie slightly more mesial in the anterolateral columns than in Gowers' tract proper.⁶

The first operation of chordotomy with division of the pain and temperature fibers was performed by Martin at Spiller's request.⁷ The patient had a malignant growth in the spinal cord with severe pain in the pelvis and lower limbs. The operation was done Jan. 19, 1911,

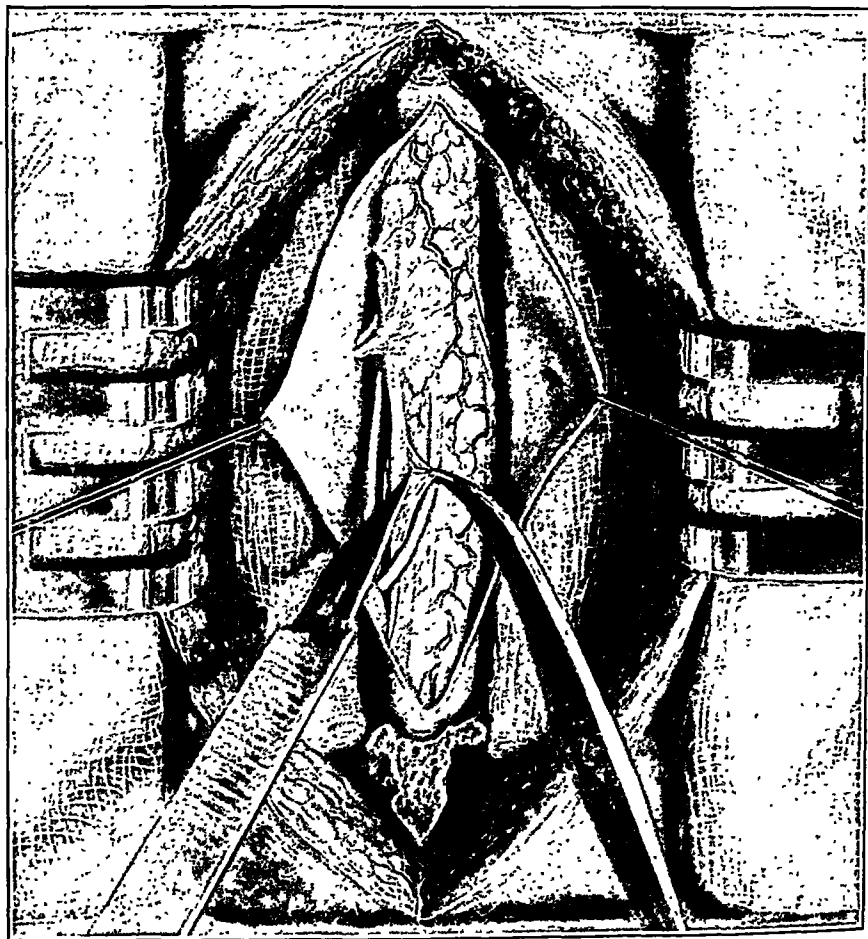


Fig. 1.—Left anterolateral tract: the arachnoid has been freed, the attachment of the dentate ligament divided and the cord rotated; the knife is about to be inserted just in front of the reflection of the dentate ligament from the cord.

both anterolateral columns being divided to a depth of about 2 mm. at a point opposite the seventh dorsal vertebra. Pain was much diminished

6. Spiller, W. G.: Remarks Before the American Neurological Association, *Arch. Neurol. & Psychiat.* 4:575 (Nov.) 1920.

7. Spiller, W. G., and Martin, Edward: The Treatment of Persistent Pain of Organic Origin in the Lower Part of the Body by Division of the Anterolateral Column of the Spinal Cord, *J. A. M. A.* 58:1489 (May 18) 1912.

and Spiller regarded the result as successful when he reexamined the patient more than a year later.

At Spiller's suggestion confirmatory experimental work was then undertaken by Cadwalader and Sweet.⁸ They came to the conclusion that sensations of pain and temperature were abolished or greatly impaired in the dogs in which they divided the anterolateral tracts.

Rothman carried out similar experiments and showed that the sensation of pain was carried in the anterior part of the lateral column. Rivers and Head proved that although there are two distinct mechanisms for the reception of painful stimuli, both these systems are grouped together in the anterolateral portions of the cord and therefore division of this tract on either side should give analgesia.

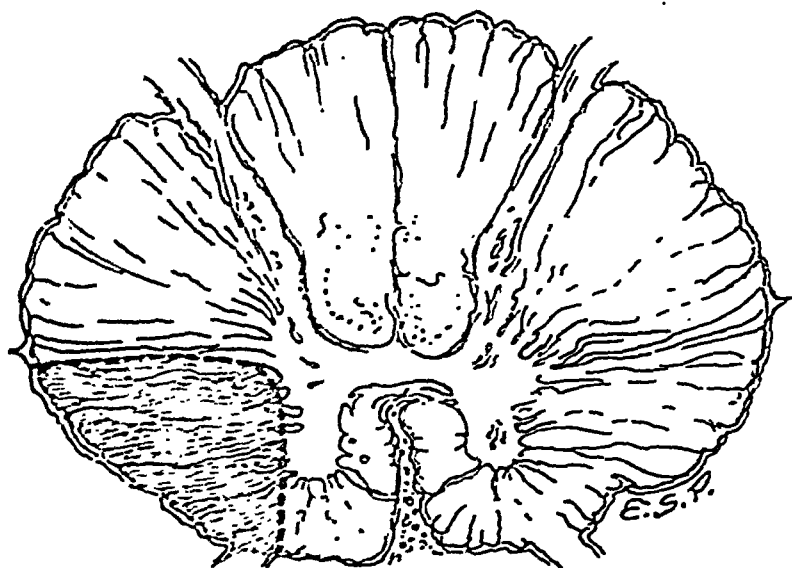


Fig. 2.—Spinal cord at level of fifth dorsal segment showing portion of cord included in section of an anterolateral tract.

The second chordotomy with section of an anterolateral column was performed in 1912 by Beer⁹ for the relief of pain due to metastases from a carcinoma of the cervix. A malignant mass could be felt on the right side of the pelvis and the patient complained of severe pain on the right side in the lumbosacral region and in the right lower extremity. Chordotomy at the level of the tenth dorsal vertebra gave complete analgesia and loss of cold perception on the right up to a line roughly horizontal with the pubes. While the pain in the back was not relieved,

8. Cadwalader, W. B., and Sweet, J. E.: Experimental Work on the Function of the Anterolateral Column of the Spinal Cord, *J. A. M. A.* 58:1490 (May 18) 1912.

9. Beer, Edwin: The Relief of Intractable and Persistent Pain Due to Metastases Pressing on Nerve Plexuses, *J. A. M. A.* 60:267 (Jan. 25) 1913.

the patient was on the whole greatly benefited as the most severe pain, which had been referred to the leg, did not recur.

Later the operation was performed by Tietze at Förster's suggestion and by Elsberg, but it did not attract the attention it deserves until Frazier¹⁰ in 1920 published a series of six cases. The results, except in one instance, were satisfactory and in this, the sixth, considerable relief was obtained. Since the operation is still comparatively new and much is yet to be learned, particularly in regard to the amount or area of analgesia obtained by cutting the anterolateral columns at various levels and at different depths, we have thought it advisable to summarize briefly the published cases. An abstract of Frazier's first series of six cases in which chordotomies were performed for the relief of pain follows.

SERIES OF SIX CASES

CASE 1 (Frazier).—The patient had a sarcoma of the spine with intense pain from the hips to the knees and cramps in the calf muscles. Complete relief followed bilateral chordotomy, 3 mm. deep, at the level of the ninth and the tenth thoracic vertebrae. Practically complete loss of pain and thermal sense was noted below the level of the first lumbar segment.

CASE 2 (Frazier).—The patient had a gunshot wound of the spine with intense pain in the left leg. Complete relief followed unilateral chordotomy between the fifth and the sixth thoracic vertebrae.

CASE 3 (Frazier).—In a case of carcinoma of the rectum, with severe pain in the rectum, the perineum and the thighs, radium treatment had given no relief from pain. Bilateral chordotomy, 2.5 mm. deep, between the levels of the ninth and the tenth thoracic vertebrae yielded "loss of thermal and pain sensation over the buttock, perineum, posterior aspect of the thigh and below the level of the knee" on the right but no loss of the thermal or pain sensations on the left. Temporary flaccid paralysis of the left lower extremity disappeared in two weeks. The pain in the perineum and rectum was completely relieved in spite of only unilateral analgesia. The results were satisfactory four years later.

CASE 4 (Frazier).—The patient suffered terrible pain in the gluteal region from a sarcoma of the thigh with pelvic metastasis; this was completely relieved by unilateral chordotomy between the seventh and the eighth thoracic vertebrae.

CASE 5 (Frazier).—The patient had pain in both lower extremities, the result of a gunshot wound of the spine. Bilateral chordotomy at the level of the sixth thoracic vertebra gave immediate complete loss of pain and temperature sensation below the umbilicus. Unfortunately the subsequent history is unavailable.

CASE 6 (Frazier).—The patient had received a shell wound of the pelvis with an injury to the sciatic nerve. There was severe pain in the right leg along the course of the nerve. A burning and shooting pain was located in the thigh from a point about 12 inches (30.4 cm.) above the knee to 3 inches (7.6 cm.) above the midpopliteal space and in the right foot. Touch, pain and temperature sensations were completely lost in the distribution of the sciatic nerve. Unilateral chordotomy between the sixth and the seventh thoracic vertebrae was performed.

10. Frazier, C. H.: Section of the Anterolateral Columns of the Spinal Cord for the Relief of Pain, *Arch. Neurol. & Psychiat.* 4:137 (Nov.) 1920.

There was a diminution of the pain sensation but not complete loss in the leg and lower part of the abdomen of the opposite side; the temperature sense was impaired over the same area. A paresthesia persisted in the sole of the right foot. The pain was relieved for three months and then returned, necessitating further surgical intervention (case 7, Frazier and Spiller).

Shortly after the publication of this article Leighton¹¹ performed four chordotomies, three for the relief of tabetic pain and one for pain resulting from spinal cord injury. His patients were much benefited.

CASE 1 (Leighton).—The patient had typical *tabes dorsalis*, with pain involving the right side of the trunk and the right leg. Unilateral chordotomy at about the level of the sixth thoracic vertebra gave complete relief from the pain in the right leg.

CASE 2 (Leighton).—The patient had traumatic myelitis in the lower thoracic region, with lancinating pains in both legs and severe pain in the abdomen. Bilateral chordotomy after removal of the laminae of the fifth, sixth and seventh thoracic vertebrae resulted in relief of pain in both legs and loss of pain and temperature sensation below the level of the twelfth thoracic segment.

CASE 3 (Leighton).—The patient had typical *tabes dorsalis*, with gastric crises and pains of lancinating character in both legs. Bilateral chordotomy between the fifth and the sixth thoracic vertebrae gave complete relief from pain in both the abdomen and the legs.

CASE 4 (Leighton).—The patient had typical *tabes dorsalis*, with shooting pains in both legs. Bilateral chordotomy after removal of the fifth, the sixth and the seventh dorsal laminae gave considerable relief for the four weeks the patient was observed. He had occasional pain in the feet and Leighton noted that apparently all the pain fibers were not divided.

Frazier and Spiller¹² in 1923 reported the following cases, seven of which were new, one, case 7, being case 6 in Frazier's previously published series.

SERIES OF EIGHT CASES

CASE 1 (Frazier and Spiller).—The patient had practically complete paralysis of both lower extremities, with attacks of excruciating pain in both legs, following a wound from a high explosive shell in the third and the fourth lumbar vertebrae. Two operations with section of the posterior nerve roots had been performed without benefit. Bilateral chordotomy, on the right at the fifth and on the left at the sixth thoracic segments, resulted in loss of subjective pain and in a delayed pain sense over the right thigh and the right side of the abdomen to the umbilicus, and a lost pain sense in the left leg and the left side of the abdomen to about 2 inches (5 cm.) below the umbilicus. The heat and cold sensations were lost up to 1 inch (2.5 cm.) above the umbilicus on the right and to about 2 inches (5 cm.) below on the left.

11. Leighton, W. E.: Section of the Anterolateral Tract of the Cord for the Relief of Intractable Pain Due to Spinal Cord Lesions, *Surg. Gynec. Obst.* **33**:246 (Sept.) 1921.

12. Frazier, C. H., and Spiller, W. G.: Section of the Anterolateral Columns of the Spinal Cord (Chordotomy), *Arch. Neurol. & Psychiat.* **9**:1 (Jan.) 1923.

CASE 2 (Frazier and Spiller).—The patient suffered agonizing pain, the result of a sarcoma of the vertebrae involving the cord at the ninth thoracic segment; this was entirely relieved by bilateral chordotomy at the level of the fifth thoracic segment. Pain sensation was lost 2 cm. below the umbilicus on the right and almost entirely over the left side of the lower part of the abdomen. The thermal sensation on the right was lost 10.5 cm. and on the left 7.5 cm. above the umbilicus.

CASE 3 (Frazier and Spiller).—The patient had metastatic carcinoma from the breast to the fifth lumbar vertebra and both iliac bones, with sharp, shooting pains in the legs and the pelvic organs. Bilateral chordotomy at about the fifth thoracic segment gave complete relief from the pain and great disturbance of the temperature sensation to a level slightly above the umbilicus. The pain sensation was largely lost over the same area. There was loss of dorsal flexion in both ankles and toes.

CASE 4 (Frazier and Spiller).—The patient had severe pain of unknown origin in the left side of the rectum and vagina and in the sole of the left foot. Section of the right anterolateral column at the level of the fourth and the fifth thoracic spinous processes gave complete relief of pain on the left side. There was a temporary paralysis of the right lower limb which remained as a permanent though slight weakness. Later, pain developed in the right side of the bladder and vagina, in the right thumb, heel and posterior half of the outer border of the right foot, necessitating chordotomy on the opposite side.

CASE 5 (Frazier and Spiller).—The patient had carcinoma of the rectum, which had been treated with radium and later by a modified Kraske's operation. Severe pain was referred to the sacrum and both legs, particularly the right. Three grains (0.19 Gm.) of morphine was required daily. Bilateral chordotomy at the level of the tenth and the eleventh thoracic vertebrae gave complete relief of pain. The areas of analgesia were not tested. The patient died from meningitis on the thirteenth day, probably as the result of severe cachexia.

CASE 6 (Frazier and Spiller).—The patient had carcinoma of the cecum, which was removed, but later an inoperable recurrence was found. Practically constant pain was felt in the right lower limb, which was aggravated by walking. Morphine was not tolerated. A left anterolateral chordotomy between the fourth and the fifth thoracic vertebrae gave relief from the pain in the right leg. Two weeks later the pain sensation was markedly impaired, but not completely lost in the whole right lower limb. It was somewhat affected up to the level of the umbilicus. The thermal sensation was lost over the entire right leg and ice was called a pin prick to 2 or 3 inches (5 or 7.6 cm.) above the umbilicus. Very hot water was sometimes recognized in the same area. Six weeks after the operation the area of impaired sensation had diminished, pain, heat and cold being recognized immediately above Poupart's ligament. Later the pain sensation returned about the knee, but was lost above this point to the inguinal region.

CASE 7 (Frazier and Spiller; case 6 in Frazier series).—The patient had suffered an injury to the sciatic nerve from a high explosive shell. First, a chordotomy relieved the pain in the thigh and foot for two or three months. It returned only in the foot. Two years later pain in the foot was still present, with impaired pain perception to about 1 inch (2.5 cm.) above the umbilicus. A unilateral chordotomy was performed at the level of the fifth thoracic vertebra, one vertebra higher than at the previous operation. The pain in the foot was not completely relieved although there was a complete loss of pain and thermal sensation up to about 1 inch above the umbilicus on the right; then pain in the thigh

along the course of the sciatic nerve returned. The pain, however, continued on the inner side of the leg from the knee to the sole. Decompression of the sciatic nerve gave some relief for only a few days, and failed of effect on the peroneal nerve. Previous chordotomies had been made to a depth of 25 mm. The operation on the left anterolateral column was made 3 mm. deep at the level of the first thoracic segment. This apparently gave relief although the pain returned at times. There evidently was a marked psychomotor element present.

CASE 8 (Frazier and Spiller).—The patient had myelitis, with sensory hyperesthesia around the upper part of the thorax. A bilateral chordotomy at the level of the first thoracic segment gave practically complete relief. Sensations for pain, heat, cold and touch were impaired, but not lost at the level of the rib to the fifth intercostal space on both sides. Sympathetic disturbances were present from the damage to the first thoracic nerve.

Our series at the University Hospital comprise a group of 200 cases, the clinical abstracts of which follow. While I performed all the operations and checked the postoperative findings, the cases have also been carefully examined by independent observers, particularly by Drs. C. D. Camp, J. L. Garvey, L. J. Foster and W. A. Smith of the neurologic department. Only the essential portions of the history and physical, neurologic and operative findings have been incorporated in the report.

We have followed the chart of Déjerine and Thomas in counting the number of a cord segment by the number of the posterior spinous process at the level of the lesion. We thus add 3 to the vertebral designation of an upper or middle dorsal posterior spinous process to designate the cord segment of the same body level; i. e., the posterior spinous process lies over the eighth dorsal segment. The common practice is to add only 2, which is approximately correct if the seventh body is considered as a landmark. However, the vertebrae can usually be palpated and for clinical use the posterior spinous process is a more convenient guide to a given level.

PHET—OF—CERVICAL

CASE 1.—Mrs. C. P., aged 40, suffered post-traumatic myelitis, extending from the breast to the lumbar vertebrae, the palsy being relieved by a bilateral chordotomy was performed.

Ten months before admission she had fallen from a horse and sustained a fracture of the cervical vertebrae. She was confined to bed for three weeks, later a fall, while going to school, resulted in a fracture of the lumbar vertebrae. The post-traumatic myelitis was characterized by a lumbar region of the extremities, which gradually extended up the legs produced the most extreme rigidity. The rigidity was relieved by the

There was a recent onset of the disease, and the symptoms were progressive. The left leg muscles showed a marked wasting, and the right leg muscles showed a marked wasting. The rigidity was relieved by the operation. The patient was discharged from the hospital, and the rigidity was relieved by the operation. The patient was discharged from the hospital, and the rigidity was relieved by the operation. The patient was discharged from the hospital, and the rigidity was relieved by the operation.

The pain was so severe and morphine gave such little relief that section of the anterolateral tracts was deemed advisable.

March 5, 1921, the posterior spinous processes and the laminae of the fifth and sixth dorsal vertebrae were removed. The right anterolateral tract was sectioned at the level of the fifth spinous process to a depth of 2.5 mm. at the pial reflection of the dentate ligament and the incision carried forward and outward to the exit of an anterior root. A similar incision was attempted on the left, but the dentate

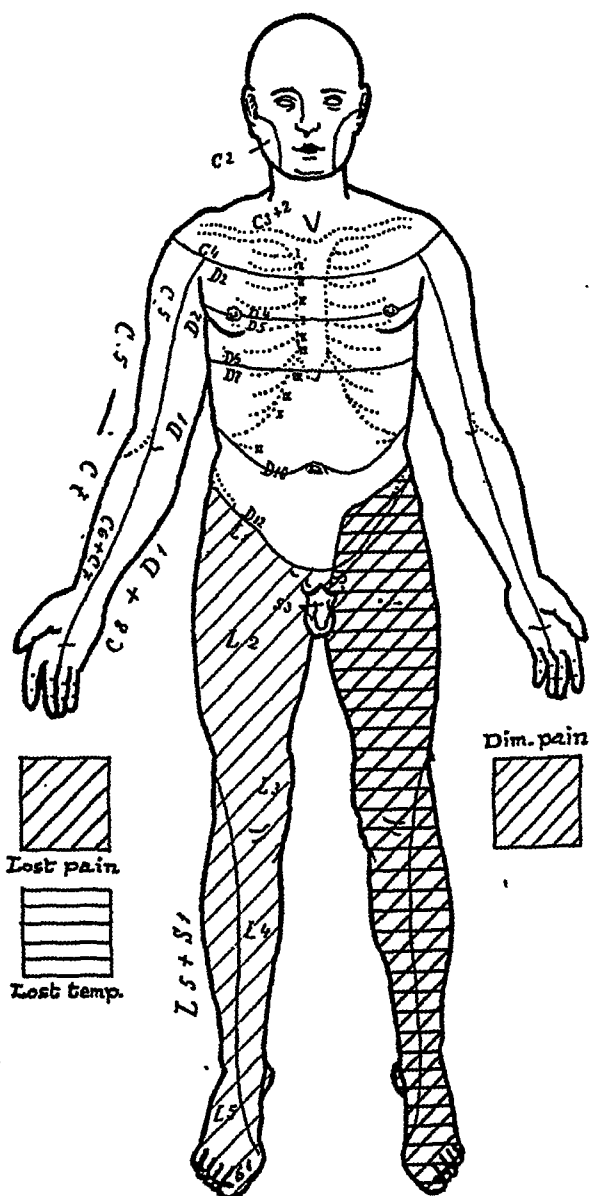
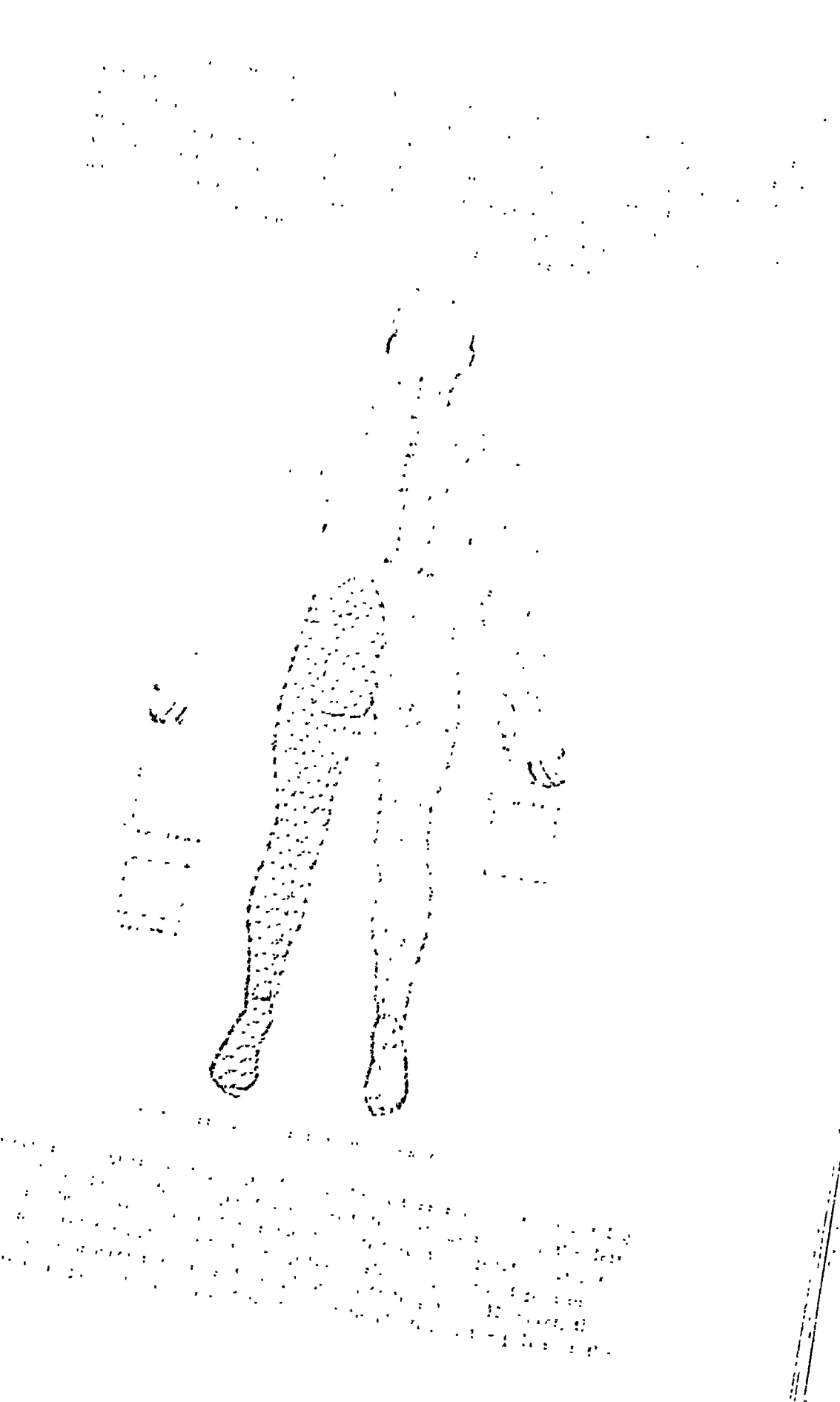


Fig. 3 (case 1).—Areas of lost pain and temperature and diminished pain eight days after bilateral chordotomy at level of eighth dorsal segment; depth, 2.5 mm. on right, slightly less on left; complete relief of pain.

ligament slipped from the forceps and our impression was that the incision did not extend as deeply as on the right.

Complete relief of the pain in the lumbar region, the pelvis and the legs was noted immediately after the operation. A neurologic examination by Dr. Camp



legs by pinching or pin prick. At times when she complained of pain, sterile hypodermic injections gave immediate relief. On other occasions, codeine appeared necessary. A report from her physician about five weeks after the operation stated that the pain had apparently returned in the left leg and hip, although in less degree. Catheterization was still necessary. Two and one-half months after the operation she was reported as complaining of much pain which appeared to be genuine, although the report added that there was no question but that she exaggerated her symptoms a great deal.

This, our first case, was encouraging but raised the question whether cutting the cord to a depth of 2.5 mm. was always sufficient. How much actual permanent relief of pain was obtained is difficult of determination. Certainly at first the relief was complete and for the twenty-four postoperative days she was in the hospital no pain could be elicited by the usual procedures. Morphine was not actually required to relieve the pain of which she regularly complained, although before operation this drug had given little relief. Whether the development of metastases at a higher level might have caused the pain referred to by her home physician is uncertain.

CASE 2.—Mrs. N. A., aged 50, had extreme pain in the lumbar region and pelvis due to carcinoma of the uterus; a bilateral chordotomy was performed.

The present trouble began about four months before admission with severe uterine hemorrhages associated with pain in the left lower quadrant and cramps across the lower part of the abdomen. Curettage showed far advanced medullary squamous cell carcinoma of the cervix. Radical cauterization with an actual cautery was performed.

Physical and neurologic examinations were negative with the exception of the extensive carcinoma of the cervix with pelvic metastases; cautery and roentgen-ray therapy gave no relief from pain. Morphine gave only partial relief. Chordotomy was advised.

July 27, 1921, the posterior spinous processes and laminae of the fifth, the sixth and the seventh dorsal vertebrae were removed. The right and the left antero-lateral tracts were sectioned at the level of the fifth spinous process, approximately the eighth dorsal segment. The incision in each column commenced at the attachment of the dentate ligament to the cord and passed directly toward the center of the cord to a depth of 3.5 mm. The knife point was then carried forward to the exit of an anterior root.

She was relieved of all pain in the lumbar region and pelvis immediately after the operation. Morphine was discontinued. Codeine was required for the first three days because of pain in the shoulders. Catheterization was necessary until the patient was able to sit up on the ninth day. All motion in the lower extremities was lost for the first two days, then motion of the toes returned. Strength gradually returned and on the tenth day the patient could move her legs; she was walking well on the nineteenth day. This temporary paralysis was probably due to the fact that the cord incision was made slightly too far posteriorly.

Neurologic examination by Dr. Camp, August 18, showed no atrophy or deformity of the legs; no paralysis; the patellar, Achilles and plantar reflexes normal on both sides. Tactile, vibratory motion and position and localization senses were normal throughout the trunk and the lower extremities. The pain and temperature senses were lost up to about 1 inch (2.5 cm.) below the umbilicus on both sides (in the tenth dorsal segment).

Although this patient had a far advanced carcinoma of the cervix which had been estimated would cause death in two or three months, her general condition improved so greatly after the terrible pains were relieved that she returned after four months asking for her previous position in the linen department. She was sleeping well, had an excellent appetite and had gained weight. She was free from pain until her death a year and nine months after the bilateral chordotomy was performed. She had no weakness in the legs and was able to go about as she pleased. The pain and temperature sensations remained lost in both lower extremities. Her daughter reported after the mother's death that her mother had "felt fine" and that her physician said that this was the only case of uterine carcinoma in his experience which had not required opiates, at least toward the end.

CASE 3.—F. P., a man, aged 66, had pelvic metastasis from a carcinoma of the prostate; a bilateral chordotomy was performed.

Three years before admission the patient had a prostate operation because of retention. One year before admission he began to have severe pain in the lower part of the abdomen and pelvis, which had grown progressively worse. For several weeks morphine in large doses had been required.

Physical and neurologic examinations were negative except for an irregular hard mass occupying the region of the prostate. This tumor was about the size of an orange and was tender on palpation. Slightly to the left of the fourth lumbar vertebra was a very tender mass about the size of a small orange. A diagnosis of far advanced carcinoma of the prostate with pelvic extension was made. The pain was excruciating and not relieved by morphine.

Jan. 9, 1922, the posterior spinous processes of the third, the fourth and the fifth vertebrae and the laminae of the fourth dorsal vertebra were removed. A bilateral chordotomy was performed at the level of the sixth dorsal segment. The incision was carried to a depth of 3 mm. and extended from the dentate ligament to the anterior roots.

The postoperative convalescence was satisfactory except that catheterization was necessary. The patient complained of no pain below the umbilicus but did have pain in the chest. On the sixth day, he complained of severe pain in the bladder region although the skin up to the umbilicus was insensitive to pain. The urethra also was analgesic. The pain in the bladder was not constant and after a few days was only occasionally referred to.

Neurologic examination by Dr. Camp, January 23, showed normal motion in both extremities; deep and superficial reflexes unchanged; senses of motion, position, touch and vibration normal, and the pain and temperature senses lost below the area supplied by the tenth dorsal segment. He could not distinguish between a pin point and a pin head below the twelfth segment. Tenderness in the tendon of Achilles was lost on both sides.

He did not require morphine after the operation to relieve his first complaint, pain in the lower part of the abdomen and the pelvis. However, pain in the chest gradually increased and morphine was finally required to give relief. The latter pain was probably due to metastasis high up in the dorsal spine although this was never proved. The pain referred to the bladder may have been, as the examining neurologist thought, complained of simply to get morphine, as the habit had already been acquired. The exact mechanism of painful sensation in the bladder is not yet known, and it is possible that pain in this region could have been present although the overlying integument was completely analgesic.

CASE 4.—Mrs. E. N., aged 35, suffered pain in the lower part of the abdomen, in the pelvis and the lumbosacral region caused by advanced carcinoma of the

uterus. A bilateral chordotomy was performed, and a second chordotomy was necessary.

She first noticed the present trouble one year before admission when she had a sudden uterine hemorrhage. A diagnosis of carcinoma of the cervix involving the body of the uterus was made at another hospital and seven radium treatments were administered. A biopsy here showed squamous cell carcinoma of the cervix. She has received roentgen-ray therapy and cauterization. For five months she had had pains in the lower part of the abdomen, in the pelvis, in the lumbosacral region and down the thighs. These pains were now severe and practically continuous. Large doses of morphine had been frequently required, but these were giving little relief at present.

Physical examination showed marked tenderness in both lower quadrants. The vaginal lymphatic glands on the right were enlarged and the neighboring vessels were greatly engorged. The cervix was replaced by a large cauliflower mass of malignant tissue which practically filled the vagina. The uterus was enlarged and fixed. The pelvis was filled with metastases. The right leg was markedly swollen with an induration about the ankle and calf. The left leg and ankle were somewhat swollen. Neurologic examination was negative.

Nov. 16, 1921, the posterior spinous processes and laminae of the second, third and fourth dorsal vertebrae were removed. The anterolateral columns at the level of the third spinous process (between the fifth and sixth dorsal segments) were sectioned to a depth of 2.5 mm., the incision extending from the attachment of the dentate ligament forward to the emergence of an anterior root. The arachnoid was much thickened and adherent to the dura and the cord, probably from some previous infection.

The patient was free from pain in the lower part of the abdomen and the lumbosacral region for ten days. Examination the day after operation showed complete loss of pain and temperature senses below the level of the eighth dorsal segment. Three days later a neurologic examination by Dr. Camp showed the pain and temperature senses returned but there was considerable delay in perception and summation phenomena were marked in the area in which they were previously lost. Tactile and vibratory sensation and sense of motion and position were normal. The umbilical reflex was normal. The knee and Achilles reflexes were increased. Plantar irritation caused flexion of the toes on each side. Bladder control was normal.

Ten days after operation she again complained of pain, principally in the right groin and leg. This pain grew progressively worse and became almost continuous; the glands in the groin had enlarged and become hot and tender. By January 10 the pain was much more severe and difficult to control with morphine. A second chordotomy was considered advisable.

Jan. 13, 1922, the posterior spinous processes and laminae of the seventh cervical and first dorsal vertebrae were removed. Bilateral sections of the anterolateral tracts at the level of the first dorsal spinous process were made to a depth of 3.5 mm. Each incision extended from the dentate ligament forward to the exit of an anterior root. Complete relief from pain in the groin and leg was experienced. Neurologic examination showed complete loss of pain and temperature sensations below the area supplied by the sixth dorsal segment on each side. Tactile sensation was unimpaired. The senses of motion and position were preserved. The vibratory sense was normal. Reflexes were unchanged. Tenderness in the Achilles tendons was lost on both sides; motion was preserved. The bladder control was normal at first, but the patient became incontinent as the disease progressed.

The temporary loss of pain and temperature sense with temporary relief of pain must be attributed to trauma without actual division of the spinal fibers involved. Such an injury just mesial to the tracts actually cut seems not only possible but probable.

CASE 5.—Mrs. J. B., aged 48, suffered from pain in the pelvis and legs caused by carcinoma of the uterus; a bilateral chordotomy was performed.

Two years before admission she first noticed a profuse, foul, yellowish vaginal discharge, occasionally blood stained. There had been frequency of urination, with occasional burning in the bladder region. For the last year, there had been severe bearing down pains with occasional sharp pain in the left lower quadrant and in the legs. In September, 1921, the cervix and uterus were cauterized. Since then the pain in the pelvis and legs had grown steadily worse. Morphine in one-half grain (0.03 Gm.) doses was now required to obtain any relief.

Physical examination showed an anemic, emaciated woman in much pain. The pelvis and lower part of the abdomen were filled with a hard, tender mass. The cervix showed a large ulcerating crater. Neurologic examination was negative. Although this patient was in a poor condition, we felt that chordotomy was justifiable since morphine was failing to give relief.

Feb. 16, 1922, the spinous processes and laminae of the third and fourth dorsal vertebrae were removed. A bilateral section of the anterolateral tracts at the level of the third spinous process (between the fifth and sixth dorsal segments) to a depth of 3 mm. extended from the dentate ligament anteriorly to the exit of the anterior roots.

Pain was immediately and completely relieved in the lower part of the abdomen, pelvis and legs. Morphine was required, however, to relieve pain between the shoulders. One-quarter grain (0.016 Gm.) doses were sufficient whereas one-half grain (0.03 Gm.) had not given relief for the previous leg pains. A neurologic examination revealed that all motion was present but that the leg movements were weaker; patellar and Achilles reflexes were present; plantar irritation caused flexion of the toes; tactile, vibratory, motion and position senses were normal. There was loss of pain and temperature senses below a line 2 inches (5 cm.) below the umbilicus.

The deep part of the incision became infected, possibly through the blood stream from the large abscess in the carcinomatous mass in the pelvis disclosed at necropsy. The patient died from meningitis on the eighth postoperative day. Necropsy showed far advanced medullary squamous cell carcinoma of the cervix uteri, which was infiltrating the bladder wall, the upper third of the vagina and all the tissues in the right side of the pelvis. The sacro-iliac plexus was infiltrated and surrounded by carcinoma. There were multiple metastases to the pelvic lymph nodes with neoplastic infiltration of the right psoas muscle; a large abscess in the carcinomatous mass on the right; early vegetative mitral endocarditis and meningitis.

CASE 6.—Mrs. C. B., aged 48, had pain due to metastasis of a breast carcinoma to the fourth lumbar vertebra; a bilateral chordotomy was performed, and was repeated because of failure to relieve pain at the first operation.

The patient had had a radical amputation of the left breast eight months before admission. A month later, pain developed in the right hip and leg which steadily grew worse and for the last five weeks had been continuous, confining the patient to bed. It was described as sharp and shooting in the right hip and as a severe burning in the right leg. Recently, shooting pains had occurred in both legs. Morphine had given little relief. The patient had lost 23 pounds (10 Kg.)

in the last six weeks. Roentgen-ray examination showed destruction of the right lower portion of the fourth lumbar vertebra, evidently from a metastatic growth.

The patient was emaciated, and held the back more or less rigidly because of extreme pain in the lumbar region on motion. The liver was definitely enlarged, hard and sensitive. The lower part of the spine was tender on pressure. There was some enlargement of the sacrum which was very sensitive. There was marked enlargement of the trochanter of the right femur. Neurologic examination was negative except for marked hyperesthesia of the right leg. Touching both legs with a piece of cotton gave the sensation of cold.

Sept. 9, 1922, the posterior spinous processes and laminae of the third, fourth and fifth dorsal vertebrae were removed. Bilateral section of the anterolateral tracts at the level of the fourth spinous process (seventh dorsal segment) was made to a depth of 3 mm. This incision extended from the dentate ligament to the emergence of an anterior root.

No relief was experienced, the pain in the hip and leg remaining unchanged. Neurologic examination showed normal tactile, vibratory, motion and position senses. The pain and temperature senses were lost only in the distribution of the great sciatic nerve on each side. Outside these areas there was no appreciable disturbance in recognition of temperature changes nor in the reception of painful stimuli. The deep and superficial reflexes were unchanged. There was no paralysis. Bladder control was normal.

No other explanation was suggested for failure to produce analgesia and thermanesthesia to a much higher level than the possibility that the spinal cord in this patient was slightly larger than the average and the pain and temperature fibers lay more than 3 mm. from the surface. We now believe that the incision should have been extended mesially through the anterior root.

Not disheartened by the previous failure, the patient begged for a second operation in the hope that she might obtain relief. It was decided to divide the cord to a greater depth, even though motor weakness resulted as this seemed preferable to her present condition. September 25, the posterior spinous processes and the laminae of the sixth and seventh dorsal vertebrae were removed, and bilateral division of the anterolateral tracts was made at the ninth dorsal segment. On the left, the section extended from just posterior to the dentate ligament forward to the exit of an anterior root and to a depth of 4 mm. A similar incision, but to a depth of 3.5 mm., was made on the right.

The pain in the hip and legs was completely relieved. Catheterization was necessary except when micturition was involuntary. Tactile, vibratory, motion and position senses were normal. Pain and temperature senses were lost on the right below a line approximately 2 inches (5 cm.) below the umbilicus (between the areas supplied by the tenth and the eleventh dorsal segments). On the left, analgesia and thermanesthesia were present below the eleventh dorsal distribution. There was complete motor paralysis in both legs until the eleventh day when some motion returned. The patellar reflexes were absent.

Three days after operation, the metastatic areas on the sacrum and great trochanter were broken down, forming deep ulcers, which, however, were non-painful. Although comfortable and relieved of all pain except for a new complaint, pain in the jaw, she failed rapidly and died the twelfth day postoperative.

Necropsy showed metastatic adenocarcinoma from the breast to the liver, the mediastinal, bronchial, suprapancreatic and retroperitoneal lymph nodes, the suprarenals, the lumbar vertebrae, sacrum and femur; a primary medullary squamous cell carcinoma in erosion of the cervix; multiple leiomyomas of the uterus; papilliferous adenoma of the left kidney; multiple emboli and hemorrhagic infarctions of the lung, and subacute spinal pachymeningitis.

If we realized the extent of the metastasis we probably would not have considered lumpectomy in this case. Before the necropsy, however, it was not possible. In the light of our present knowledge, we would not have stated the section of the anterolateral tracts so far as the right leg was concerned. On the other hand, we have carried the incision deeper in the left tract to the point actually involving an anterior root at the third dorsal level so that there would not have actually destroyed all the posterior roots of the posterior horn as spinal cords vary in size, even at the same level.

March 1, 1923, a lumpectomy of the sacral, lumbosacral and sacral nerves due to a metastasis of the first leg with spinal metastases, a bilateral chordotomy was performed.

By December, 1922, the left foot had been quite below a lumpectomy. One year before the operation the left leg was amputated at a low level for a round cell carcinoma. The pain had been in the lower part of the leg, involved the right leg and lower part of the back. It was sharp at first, then of a character undulating in nature, but was quite constant in character. There was numbness in the leg. Although the left leg had been amputated, she still felt the pain, a hot glow in it. Morphine had been administered in large doses, but it was still the pain had been so excruciating that she had given up. After the operation the hyperaesthesia gave practically no relief. Deep anesthesia during the operation was needed.

Two days before the operation a patient, a married girl, evidently in great pain. The pain was in the right leg, but it was not a sharp pain. The left leg was amputated. The right patellar reflex was normal. The tendon of Achilles reflex was normal. There was numbness of the toes on plantar irritation. The sensory system and pain system were not reliable. The vibratory sense in the left leg was normal. There was marked weakness in all the movements of the right leg and foot. The sensory and pain from a pin point were felt normally but the patient stated that the leg of the foot felt "numb" to a pin point. The sense of the excruciating pain, which was no longer relieved by morphine, a chloroform was felt, numbed. This was with the full understanding that the patient's condition was poor and that she might die from the malignancy at any time. Her condition was so painful that any one seeing her and knowing that it was almost impossible for her to obtain any sleep would have felt that operation was probable.

Feb. 21, 1923, a lumpectomy was performed, with removal of the posterior spinous processes of the second, third and fourth vertebrae and of the laminae of the third dorsal vertebra. Section of the anterolateral tract to a depth of 2.5 mm. on the right and 3 mm. on the left was made.

She was immediately and completely relieved of the terrible pain in the lower back, right leg, and that referred to the amputated leg, but had considerable pain in the chest. There was complete loss of pain and temperature sensations on the right side downward from a line about 2 inches (5 cm.) below the umbilicus (approximately the eleventh dorsal level). On the left, there was marked impairment in the recognition of painful stimuli but not a complete loss. The temperature sense was lost below the twelfth dorsal level on the left. Tactile sensations were normal throughout. The motion was the same as before operation. The right patellar reflex was normal. Catheterization was necessary except when the patient had involuntary micturition. She had had a septic temperature for some time before operation. After chordotomy the fever remained about as before for

several days; the incision then appeared infected for the first time. No attempt at healing was in evidence when the superficial part of the wound was opened. No symptoms of meningitis developed but death took place on the eleventh day postoperative. Necropsy showed a fibrinopurulent meningitis; multiple infarcts of the brain; multiple metastases of an alveolar round cell sarcoma in the cranial bones, dura mater, lungs, pleura, mediastinum, heart muscle, bronchial and retroperitoneal lymph nodes.

It is questionable whether this death was due to the beginning meningitis. There were no meningeal symptoms and adequate cause for death from metastases was evident. Operation probably hastened the end, but did make the last few days more comfortable.

CASE 8.—R. H., a man, aged 40, had pain due to spinal metastasis from adenocarcinoma of the bronchus; a bilateral chordotomy was performed.

His present trouble started a year ago with pain in the right hip. This gradually extended down posterior to the right thigh and calf and was made worse when the patient moved or bent forward. Flexion of the leg gave relief. Six months later, he developed a similar pain in the left thigh and leg. The pain now was practically constant; he took as much as 3 grains (0.19 Gm.) of morphine at a time.

Physical examination was essentially negative except for atrophy of the right lower extremity. Neurologic examination showed increased patellar and Achilles reflexes; an abortive ankle clonus on both sides; no sensory changes. Roentgen-ray examination showed metastases in the fifth lumbar vertebra, in the upper portion of the sacrum and in the region of the left sacro-iliac joint. A dense mass was also seen at the hilum of the left lung.

The pain was severe in both legs, morphine giving only partial relief. Some pain was felt in the chest. Deep roentgen-ray therapy to the chest and lumbosacral region failed to give any relief. Accordingly, chordotomy was advised.

May 28, 1923, a laminectomy was performed with removal of the posterior spinous processes and laminae of the fourth and fifth dorsal vertebrae. Very extensive adhesions between the pia and the arachnoid and to a somewhat less extent to the dura, were found. The spinal cord was yellowish and very stiff as if infiltrated, making rotation difficult. The arachnoid could not be separated from the pia; neither could the attachment of the dentate ligament to the cord be exactly determined. The anterior and posterior nerve roots were adherent to the pia, making it almost impossible in the mass of adhesions to distinguish their exact points of emergence. The knife was inserted at a point approximately halfway between what was considered the points of emergence of the anterior and the posterior roots. The incision was carried to a depth of 3 mm. and forward to the exit of an anterior root. A similar section of the cord was performed on the opposite side.

Following the operation the patient was completely relieved of pain in the legs but complained of considerable pain in the chest. This increased in severity for a time, requiring daily doses of morphine. The chest pain practically disappeared about three weeks after the operation but recurred later, requiring frequent hypodermic injections. Neurologic examination showed complete loss of both pain and temperature senses up to the level of the eleventh dorsal segment. Motor function in both legs was completely lost at first but gradually returned so that he was able to get into a wheel chair four weeks later; however, he never got back sufficient strength to walk. The knee and tendon of Achilles reflexes were

markedly increased as before the operation. Tenderness in the Achilles tendon was lost. There was no change in the tactile, vibratory, motion or position senses. The patient had been catheterized before operation and this had to be continued. He gradually grew weaker and died, July 7. Necropsy disclosed a primary medullary adenocarcinoma of the bronchus of the upper lobe of the left lung. There were metastases throughout the left lung and in the bronchial, mediastinal, lower cervical, prevertebral and retroperitoneal lymph nodes, in the right lung, liver, lower lumbar vertebrae and sacrum.

While chordotomy gave this man complete relief from unbearable pain in the legs, it should not have resulted in the motor weakness noted. Possibly this motor loss would have disappeared had the patient survived for a longer period. He was confined to bed before the operation so was not, in his opinion, made worse by the paralysis of the legs. As the exact location of the dentate ligament could not be determined, it is probable that the incision was made too far posteriorly.

CASE 9.—S. R., a man, aged 24, had traumatic sciatic neuralgia associated with partial avulsion of the lumbosacral plexus; a unilateral chordotomy was performed.

The patient was well until two months before admission when he was run over by a farm tractor. The right hip was dislocated but no other injury to the soft parts or bone was discernible. The dislocation of the hip was immediately reduced but he had been unable to walk since because of excruciating pain on movement of the right leg. This developed three or four days after the accident and was described as a constant, severe burning, associated with sharp, stabbing pains. It was confined to the lower right leg and foot. The latter was so hypersensitive that he could not bear the weight of a sheet on it. Touching the foot markedly aggravated the pain.

Physical and neurologic examinations were negative except that there was some atrophy of the glutei muscles and the right great trochanter was more prominent than the left; there was some limitation on extension of the right hip; there were atrophy of the muscles of the right lower leg and atrophic changes in the skin on the dorsum of the right foot. Pain in the popliteal space prevented extension of the right leg at the knee beyond a right angle. The calf of the leg was tender on pressure and all the voluntary movements at the right ankle joint were lost. He could not extend the toes but could flex them slightly. Some sense of motion and position was lost in the right toes. A tuning fork vibration caused pain in the right ankle. Tenderness on pressure was noted along the right sciatic nerve. There was lost tactile sensation and marked hyperalgesia over the dorsum of the right foot and the external surface of the leg about halfway to the knee. The tactile sense was practically lost and the pain sense was greatly increased over the plantar surface of the right foot (fig. 5). There was evident continuous pain in the right foot and the lower leg.

This boy was completely incapacitated and suffering severely. Morphine given hypodermically had been required three or four times daily. The lesion evidently was in the lumbosacral plexus. A unilateral chordotomy seemed to offer the best measure of relief. The only alternative procedure was rhizotomy of the posterior roots.

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July 6, 1923, the posterior spinous processes and the laminae of the fourth and fifth dorsal vertebrae were removed. The left anterolateral column was divided between the dentate ligament and the anterior roots at the level of the fourth dorsal spinous process (the seventh dorsal segment). The incision just in front of the attachment of the dentate ligament extended to a depth of 3 mm.

The postoperative convalescence was satisfactory. The pain was immediately relieved in the leg and foot. The day following operation, he was able to extend

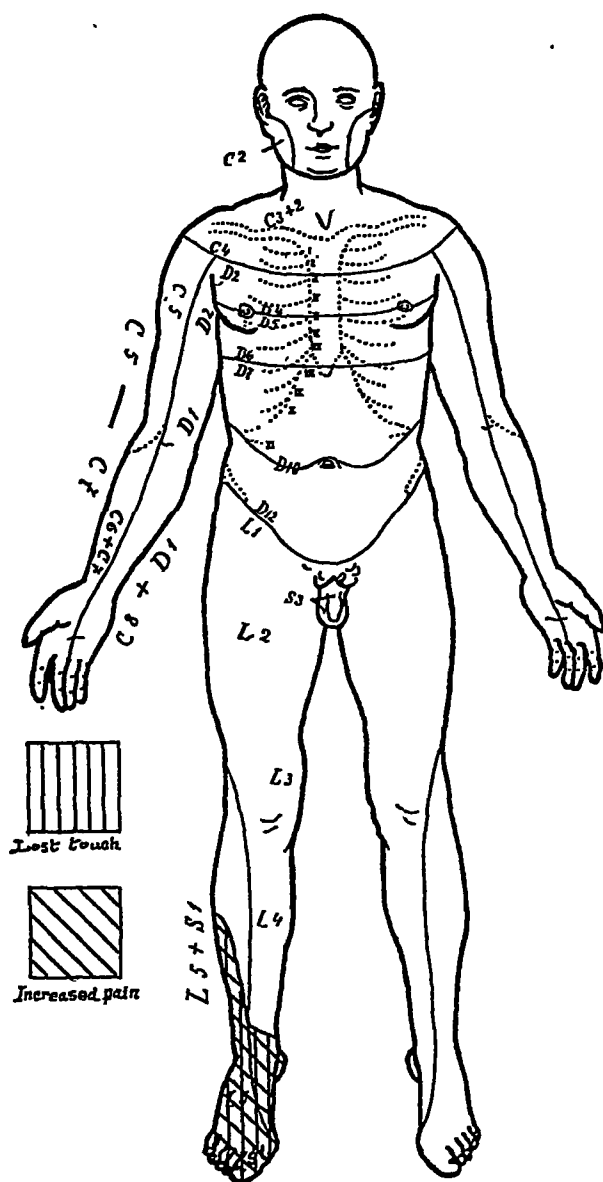


Fig. 5 (case 9).—Areas of lost touch and increased pain before operation when there were tactile anesthesia and hyperalgesia with excruciating pain in right leg.

the right leg at the hip and the knee; this had been impossible before because of induced pain. On the eighth day he was up and around in a wheel chair with a shoe on for the first time since the accident. The bladder control was not affected.

A neurologic examination, July 16, showed no change in the muscles previously paralyzed. All other movements were normal. No limitation was noted in the

extension of the leg. The tendon of Achilles tenderness was lost on the right, and the sense of motion and position of the toes was lost on the right. There were analgesia and thermanesthesia below a line around the thigh about 4 inches (10.1 cm.) above the right knee (fig. 4). The tactile sensation was lost over the same area as before. The vibratory sense was considerably diminished at the right ankle. All the tendon reflexes were normal except for the lost right Achilles

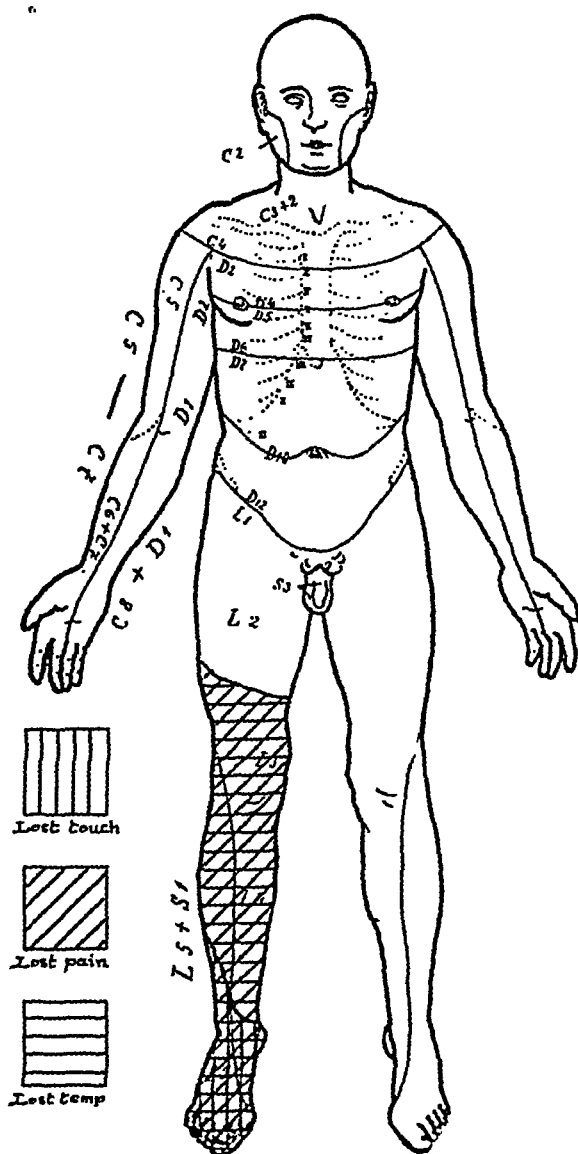


Fig. 6 (case 9).—Areas of lost touch, pain and temperature ten days after section of left anterolateral tract at seventh dorsal segment; depth, 3 mm.; complete relief of pain.

tendon reflex. Plantar irritation caused flexion of the toes on the left; there was no movement on the right.

A letter, November 16, stated that he had the sensation as of a swarm of ants running over the right foot when he lay down and that he wore an overshoe rather than a regular shoe because the foot "seemed sore."

He returned for examination, Feb. 26, 1924, reporting that he had been able to do some work, had gained 40 pounds (18.1 Kg.) in weight and was quite comfortable. Neurologic examination showed atrophy of the right glutei muscles and of the muscles of the right leg. All the tendon reflexes were normal except the lost Achilles tendon jerk. Foot drop still was present. Analgesia and thermanesthesia were present below a line about 3 inches (7.6 cm.) above the right

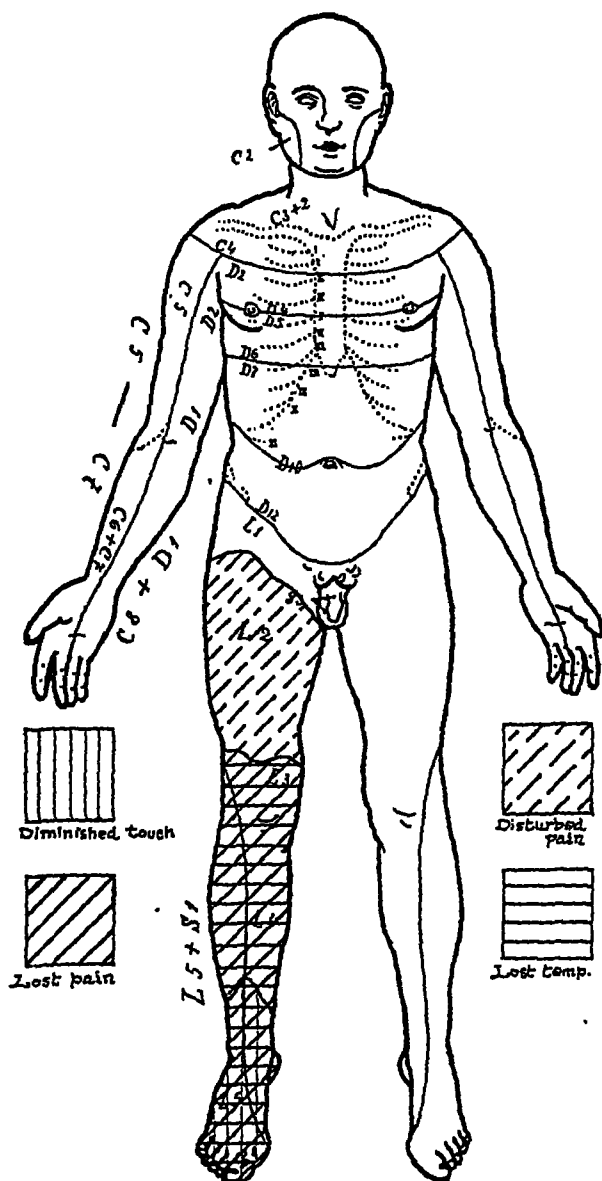


Fig. 7 (case 9).—Areas of diminished touch, lost and disturbed pain and lost temperature eight months after left chordotomy, 3 mm. deep at seventh dorsal segment.

knee. The tactile sense was lost or greatly diminished in the foot and ankle as before. Above the area of lost pain and temperature sense was a band extending nearly to the groin in which the pain sense was preserved, but not normal, a pin point being felt as a flat knife edge (figs. 7 and 8).

The last report, May 18, 1924, stated that the atrophy previously noted was progressing. Apparently no pain was felt. He expressed great appreciation for the relief afforded him.

Fortunately the pain in this case was referred only to the lower part of the leg and foot. Had the pain been in the lower back or pelvis, complete relief would not have been obtained; this, in spite of the fact that section of the anterolateral column was made at approximately the seventh dorsal segment. We now believe that the fibers

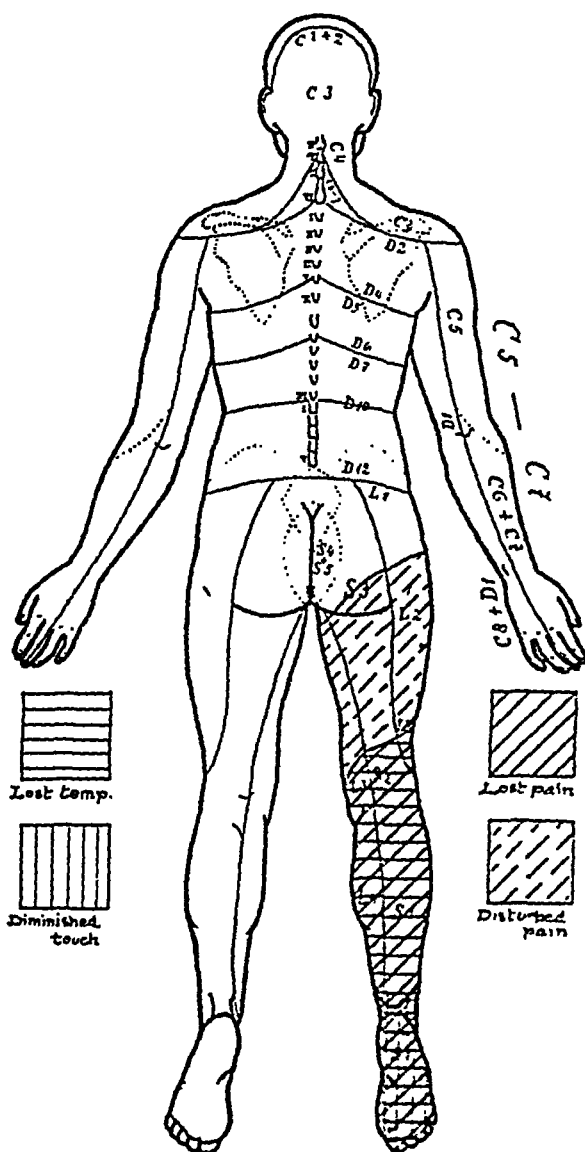


Fig. 8 (case 9).—Back view of patient.

carrying pain and temperature sensations from the thigh and lower abdominal region lie more anteriorly and mesially than those from the lower leg and foot. Had the section been made deeper at the emergence of the anterior root, the area of analgesia would have been much higher.

CASE 10.—Mrs. C. B., aged 28, suffered pains in the pelvis and lower legs from carcinoma of the uterus; a bilateral chordotomy was performed.

The present trouble began nine months before admission with shooting pains down both legs. Carcinoma of the cervix was treated with radium and the pains were relieved. The pain returned a month later but was again relieved by radium. For the last four months there had been steady pain in the groin and for one month, in the legs. After the radium treatments, the patient had a curettage and deep roentgen-ray therapy. Morphine in increasing doses had been required and now did not control the pain.

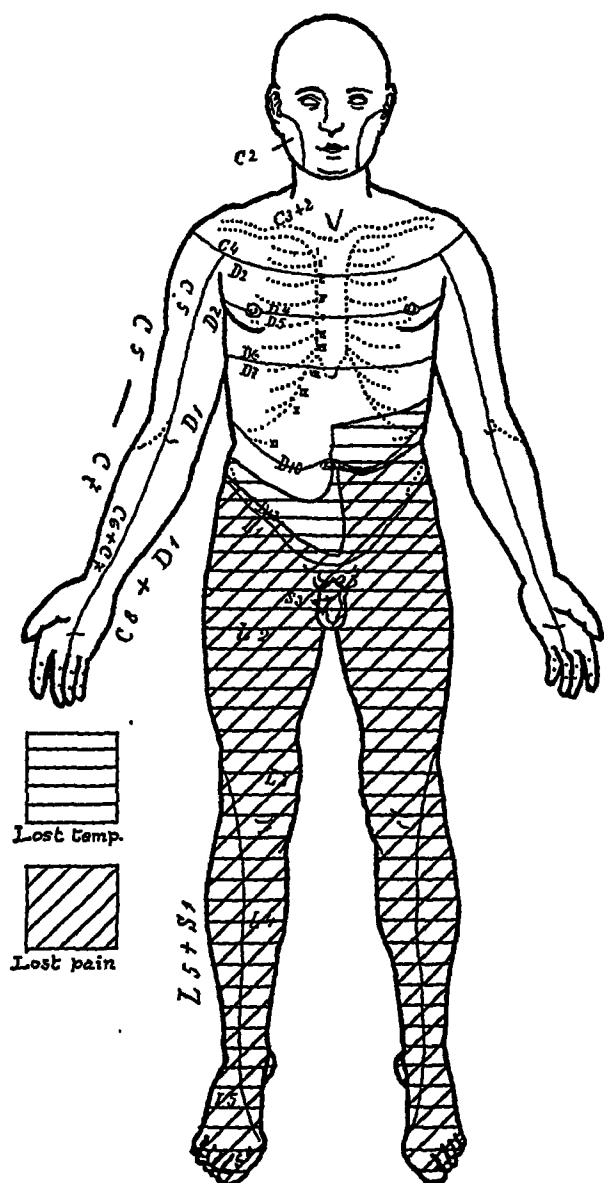


Fig. 9 (case 10).—Areas of lost temperature and pain four days after bilateral chordotomy, 3 mm. deep, at sixth dorsal segment; complete relief of pain; difference in levels of analgesia and thermanesthesia should be noted.

Physical and neurologic examinations were negative except for extreme weakness and the extensive carcinoma of the uterine cervix with pelvic metastases. A chordotomy was advised because of excruciating pain in the lower back, pelvis and both legs, uncontrolled by morphine.

Nov. 10, 1923, the posterior spinous processes and laminae of the third and fourth dorsal vertebrae were removed. A bilateral chordotomy at a level about midway between the laminae of the third and fourth dorsal vertebrae divided the anterolateral tracts in the sixth dorsal segment. The incisions extended 3 mm. in depth just in front of the dentate ligaments and were carried forward to the anterior roots.

She was completely relieved of pain, but immediately after the operation she had marked weakness in the muscles of both legs; the toes, however, could be moved normally. Urination was involuntary but the patient knew when she was urinating.

Neurologic examination, November 14, by Dr. Camp showed that the patient could make all the movements of both legs with some incoordination. The umbilical, patellar and Achilles tendon reflexes were lost. Plantar irritation caused flexion on the right, extension on the left. The pain sense was lost below the inguinal region on the right and below the umbilicus on the left. The tendon of Achilles tenderness was lost on both sides. The temperature sense was lost to a higher level than the pain sense; it was lost on the left to halfway between the umbilicus and the inguinal region, and on the right to a level about 3 inches (7.6 cm.) above the umbilicus (fig. 9). The senses of motion, position and localization were preserved; tactile and vibratory sensibilities were normal.

December 17, the patient was completely free from pain, but still weak from additional uterine hemorrhages. The knee and Achilles tendon reflexes were present on the left, absent on the right. The patient could flex the right thigh but not extend it. The left leg movements were normal. Plantar irritation caused extension on both sides. The senses of motion and position were normal; the vibratory sense was lost in the ankles. The tendon of Achilles tenderness was lost. The tactile sense was normal. The area of analgesia extended to just above the inguinal line on the right and to 2 inches (5 cm.) below the umbilicus on the left.

The motor weakness must have been due to encroachment on the crossed pyramidal tracts just posterior to the dentate ligament. A point of interest was the difference in levels of analgesia and thermanesthesia, the latter being at least one segment higher.

CASE 11.—Mrs. M. A., aged 34, had pain due to carcinoma of the cervix; a bilateral chordotomy was performed.

The present trouble began a year before admission following a miscarriage. The patient immediately had a profuse, foul, sometimes blood stained vaginal discharge, which had persisted. Backache and burning and itching around the vagina soon developed. The pain had increased in intensity and was confined largely to the lower part of the abdomen, at times passing down both legs. She had had actual cauterization of the cervix and uterus followed by deep roentgen-ray therapy; this had stopped the uterine hemorrhages but had not influenced the pain. The pathologic diagnosis was far advanced medullary squamous cell carcinoma of the cervix.

Physical examination was essentially negative with the exception of the extensive crater in the cervix and uterus with pelvic extension and metastases. A neurologic examination was negative. A chordotomy was advised.

Nov. 24, 1923, the posterior spinous processes and the laminae of the fourth and fifth dorsal vertebrae were removed, and bilateral section was made of the anterolateral tracts at the level of the seventh dorsal segment between the third

and the fifth spinous processes). The incisions were made to a depth of 3 mm., just in front of the reflection of the dentate ligament, and were carried outward and forward, emerging at an anterior root on each side.

The patient was completely relieved of pain. A neurologic examination by Dr. Camp, November 28, showed no motor weakness in the extremities. The knee and Achilles tendon reflexes were normal. Plantar irritation caused flexion of the toes on each side, and there was a lively tickle sense on both sides. The senses of motion and position were normal. The tendon of Achilles tenderness was lost on both sides. Sensation to a pin point was variable. It was felt acutely in spots and was entirely absent in surrounding spots. Both plantar surfaces were completely analgesic in spite of which the tickle sense was preserved. The loss of the pain sense while incomplete extended to the umbilicus. The patient differentiated heat and cold normally over the abdomen, in the right leg and on the outer side of the left thigh. The thermal sense was completely lost on the inner side of the left thigh and below the knee. The tactile sense was normal. She stated that her pain was entirely relieved by the operation.

Feb. 21, 1924, the patient was free from pain. The results of the neurologic examination were practically the same. A letter, March 7, 1924, stated that severe pain had developed throughout the back, especially sharp in the lumbar region, radiating to the right hip, and that she was growing much weaker and was no longer able to be about. It is possible that this new pain was due to metastases at a higher level, especially since the pain was referred higher in the back than before.

CASE 12.—H. P., a man, aged 24, had pain due to sarcoma of the femur; a bilateral chordotomy was performed, and the second and third operation, the last combined with rhizotomy.

This young man entered the hospital because of excruciating pain in the left leg and the right orbit. He first noticed pain in his left hip one year before admission. The pain was piercing and sharp in character, and worse when he was using the leg. It had steadily grown more severe, involving both legs and was now practically constant, requiring morphine in large doses. Examination revealed a right exophthalmos, apparently due to a metastasis in the posterior part of the orbit. A large fusiform swelling of the left thigh was shown by roentgen-ray examination to be a periosteal sarcoma involving the upper third of the femur. A neurologic examination was negative. Roentgen-ray therapy relieved pain in the right eye, but had no influence on the pain in the legs.

Nov. 24, 1923, a laminectomy was performed, with removal of the posterior spinous processes and laminae of the third and fourth dorsal vertebrae. A bilateral chordotomy at the level of the sixth dorsal segment was done. The incisions extended 3 mm. deep and emerged at the exit of an anterior root on each side.

A neurologic examination, November 28, showed the umbilical, cremasteric, patellar and Achilles tendon reflexes normal. Plantar irritation caused flexion on both sides. There was no loss of sense of touch, vibration, motion or position. The tendon of Achilles tenderness was lost on both sides. No pain was felt from a pin prick on the outer and posterior aspects of both legs from just below the knee to the sole of the foot. The patient made frequent mistakes in discriminating between a pin point and a pin head below the knee on the left. On the right leg, he could not discriminate temperature changes up to the groin. No motor impairment was noted.

The patient continued to have pain although morphine was not as frequently required. Examination, December 19, showed practically the same findings as given above. The analgesia is shown in figures 10 and 11. Roentgen-ray therapy continued to relieve the pain in the head but not in the legs. Accordingly, a second chordotomy was performed.

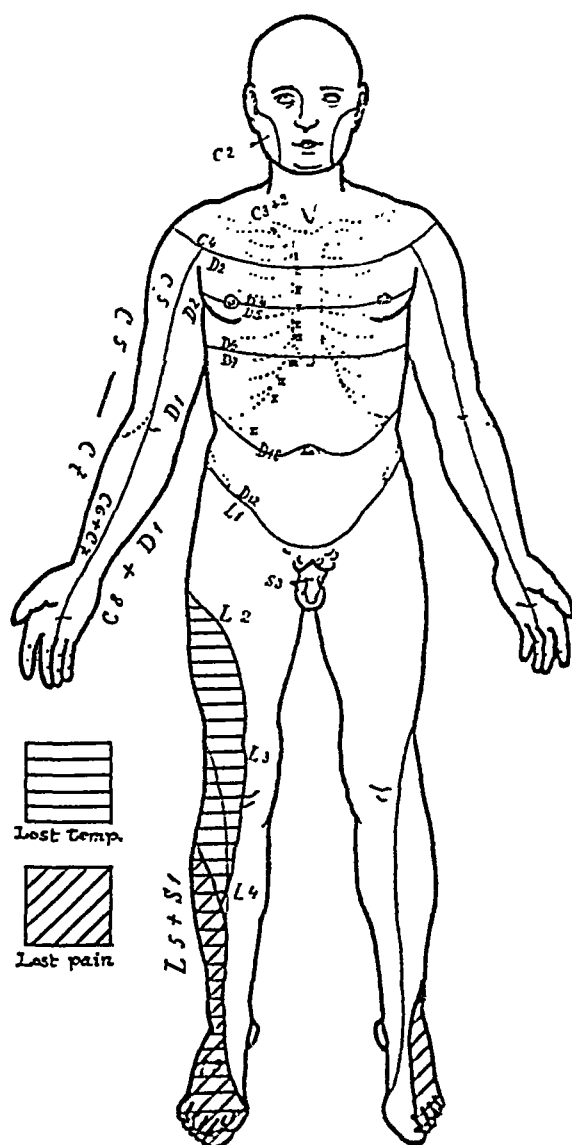


Fig. 10 (case 12).—Areas of lost temperature and pain twenty-one days after bilateral chordotomy, 3 mm. deep, at sixth dorsal segment; section extended to lateral side of motor root; second chordotomy 3 mm. deep at level of third dorsal segment made no further change in sensory findings.

December 20, a second laminectomy was performed, with removal of the posterior spinous processes and the laminae of the first and second dorsal vertebrae, and a bilateral chordotomy was done at the level of the third dorsal segment. The incision on either side extended to a depth of 3 mm. and entered lateral motor root.

A neurologic examination showed no change from the findings after the first chordotomy. The patient still complained of pain, especially in the region of the tumor and in the chest. However, morphine was not as frequently required and many times he had a good night after taking acetylsalicylic acid and barbitol. The tumor grew rapidly and, in the latter part of January, the pain increased in severity again. He begged for another spinal operation as he felt that he had been somewhat relieved by the previous chordotomies.

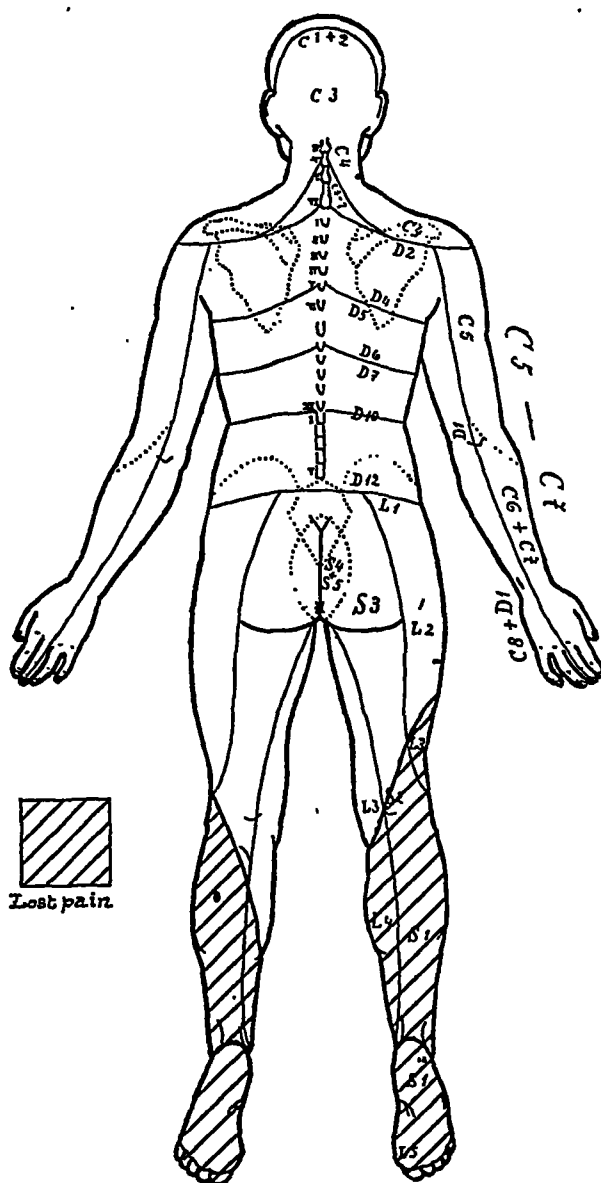


Fig. 11 (case 12).—Back view of patient.

A third operation was performed Feb. 11, 1924. The posterior spinous processes and laminae of the sixth, seventh and eighth dorsal vertebrae were removed and a bilateral chordotomy was performed at the level of the ninth dorsal segment. The knife was inserted to a depth of 3.5 mm. directly medial from the insertion of the dentate ligament and carried forward to the emergence of an anterior root. The posterior roots exposed in the operative field were divided. These were the ninth, tenth, eleventh and the upper fibers of the twelfth thoracic root.

The patient was completely relieved of the pain in both legs and up to about 2 inches (5 cm.) above the umbilicus. He still asked for morphine but after a week of satisfactory sterile hypodermic injections, the nature of his medication was explained and no further hypodermic treatments or morphine by mouth were requested.

A neurologic examination was made, February 23, showing both abdominal, the left knee and both Achilles tendon reflexes lost. There was ankle clonus on

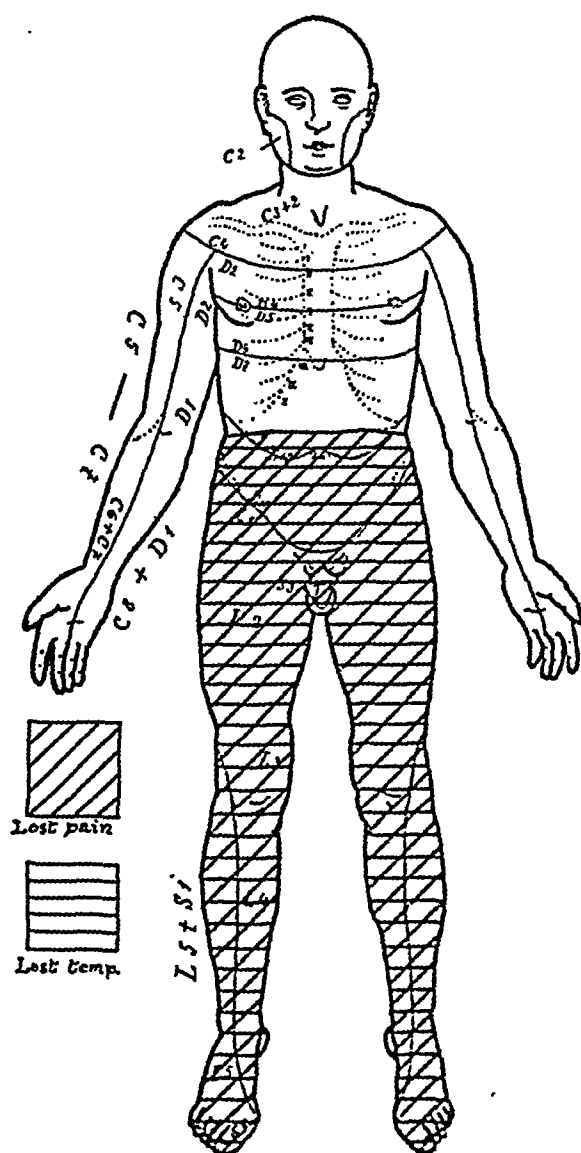


Fig. 12 (case 12).—Areas of lost pain and temperature eleven days after third bilateral chordotomy; section of anterolateral tracts, 3.5 mm. deep, at level of ninth dorsal segment. Because of two previous failures to relieve pain and to insure a higher level of analgesia, bilateral rhizotomy of ninth, tenth, eleventh and upper fibers of the twelfth posterior thoracic roots was combined with third chordotomy; complete relief was given.

the right, a positive Babinski reflex on the left. The tenderness of both Achilles tendons was lost. The tactile and vibratory senses as well as those of motion and position were normal in the legs. There was loss of pain and

temperature sense below the eighth dorsal segment (fig. 10). The patient was unable to flex the right ankle; all other motions were preserved.

He remained very comfortable except for a return of pain in the right eye which was immediately relieved by roentgen-ray treatment. Occasional urinary incontinence was noted. He died, April 9, 1924. Necropsy showed primary small spindle cell sarcoma of the left femur with metastases in the cranium, ribs, lungs and pleura, and early bronchopneumonia.

Why this patient was not completely relieved by section of the cord to the usual depth is not clear. It is possible that his cord was somewhat larger than normal or that the pain tracts were less superficial than usual. Division of the tracts only 0.5 mm. more mesially gave complete relief in the legs. The division of the posterior roots was done to insure complete loss of pain in the pelvis and lower abdomen.

CASE 13.—Mrs. M. J., aged 55, had pain in the lumbosacral region and pelvis due to advanced carcinoma of the uterus, for which a bilateral chordotomy was done.

Since an operation on the uterus in August, 1923, she had suffered much pain in both lower quadrants and in the lumbosacral region. The pain was intense, sharp, stabbing in character and frequently radiated upward. Morphine had been required at least three times daily.

Physical and neurologic examinations were negative for present consideration except for far advanced carcinoma of the uterus with extensive pelvic metastases. The patient had had deep roentgen-ray therapy without having the pain relieved, and morphine gave only partial relief.

Jan. 10, 1924, a laminectomy was performed, with removal of the posterior spinous processes and the laminae of the fourth and fifth dorsal vertebrae. A bilateral chordotomy at the level of the seventh dorsal segment was also done. The incision extended to a depth of 3 mm. and anteriorly to the emergence of an anterior root.

Postoperative convalescence was satisfactory. There was no pain in the lower part of the abdomen, the lumbosacral or pelvic regions since the operation. Catheterization was necessary for the first four days. There was some pain in the region of the operation and of the sternum, which lasted only a few days.

A neurologic examination was made January 11. The patient stated that she had none of her previous pain. All motion was preserved except for flexion of the left leg at the knee. She moved both ankles and the toes of both feet. Her sense of motion, position and vibration was normal. A light touch was felt and localized perfectly. The right patellar jerk was normal; the left was not obtained. Neither Achilles jerk was obtained. Tendon of Achilles tenderness was present. Pain and temperature senses were lost on both sides below the umbilicus. Plantar irritation gave no movement on the right, slight flexion on the left.

Examination, January 23, showed both patellar and both Achilles reflexes normal. The abdominal reflex was not obtained. Plantar irritation caused flexion on the right, unquestionable extension on the left. The area of lost pain and temperature was diminished since the first examination; there was now complete loss below the eleventh dorsal segment on the right and on the left below the twelfth dorsal on the median half of the posterior surface of the buttocks and thigh

(sacral 1, 2, 3) and of the leg below the knee (lumbar 4, 5, sacral 1) (fig. 13). She complained of some pain above the iliac crest and anterior to the superior spine on the left. All motion was now normal.

At the time of discharge she had no pain, was gaining and had overcome the morphine habit. Later examination showed no change from the foregoing findings: she was still free from pain.

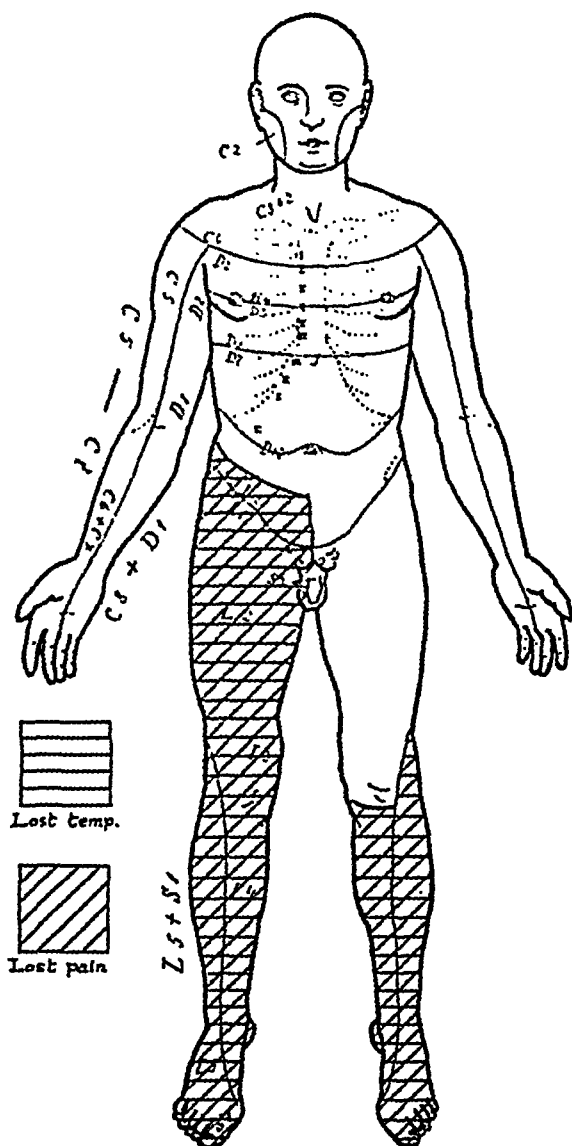


Fig. 13 (case 13).—Areas of lost pain and temperature thirteen days after bilateral chordotomy, 3 mm. deep, in seventh dorsal segment; complete relief of pain. The day after the operation pain and temperature were lost on both sides below the umbilicus. The area of analgesia and thermanesthesia generally diminishes slightly, but this is an extreme example.

CASE 14.—Mrs. E. C., aged 60, had pain due to a retroperitoneal neoplasm; a unilateral chordotomy with rhizotomy was performed.

A year before admission she had been operated on for an abdominal tumor, which was not removed. For some time previous to this she had had severe

pains in the left side of the abdomen and lumbar region. A second operation six months before admission showed a large, inoperable tumor, apparently originating retroperitoneally in the left upper quadrant. The pains had grown progressively worse, confining her to bed. They occurred almost constantly and were described as sharp and shooting in character, radiating throughout the left side of the abdomen and lumbar region, sometimes down the left leg.

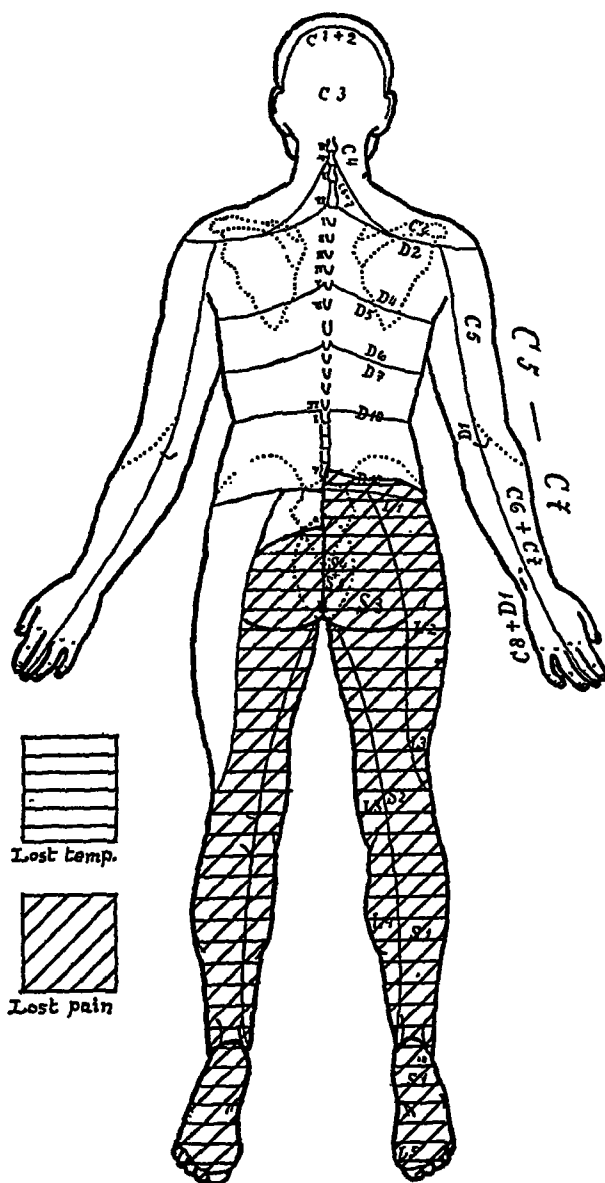


Fig. 14 (case 13).—Back view of patient.

A neurologic examination was absolutely negative. The physical and roentgen-ray examinations disclosed nothing pertinent to this study beyond the large tumor in the left side of the upper part of the abdomen. Deep roentgen-ray therapy gave no relief. Morphine was required constantly and even then did not afford an adequate measure of relief. Chordotomy combined with rhizotomy was therefore advised.

Feb. 8, 1924, a laminectomy was performed with removal of the posterior spinous processes and the laminae of the fifth, sixth and seventh dorsal vertebrae. The right anterolateral tract was divided at the eighth dorsal segment from just anterior to the pial reflection of the dentate ligament to the emergence of an anterior root, the incision being carried to a depth of 3 mm. The sixth, seventh, eighth and ninth posterior roots on the left were divided to insure analgesia slightly above the abdomen.

Postoperative convalescence was satisfactory. There was no pain in the left side of the abdomen, the left lumbar region or the left leg. The patient complained for the first time of some pain in the right side of the abdomen and, for a few days, of pain in the right leg. Catheterization was necessary much of the time although at times she voided naturally.

A neurologic examination, February 26, showed a weakness in the right leg. The left knee jerk was normal, the right markedly diminished. The left Achilles tendon jerk was normal, the right diminished. Plantar irritation caused extension on both sides. The pain sense was lost from just below the nipple line (sixth segment) to the end of the toes on the left. The temperature sense was lost below the tenth dorsal segment. Apparently there was a much wider overlapping of the temperature than the pain fibers in the skin. The tactile, motion, position and vibratory senses were preserved in both legs. The tactile sense was lost in the narrow band above the middle of the abdomen (approximately the eighth segment) on the left. On the right side at about the ninth rib anteriorly was a band of lost pain sensation.

Reports from the patient for several months showed no return of the pain in the left side of the abdomen, the lumbar region or the leg. From time to time she had pain in the right side of the abdomen. We believe that the posterior roots on the right side should have been cut although a bilateral chordotomy was scarcely indicated. Motion in the right leg was gradually improved.

CASE 15.—Mrs. M. H., aged 37, had pain in the lower abdomen and back from carcinoma of the uterus; a bilateral chordotomy was performed.

About four months before admission the patient developed pain in the lower part of the abdomen and the lower lumbar region. It had been almost continuous since and was described as sometimes sharp, at other times dull in character. Recently the pain had become extremely severe, referred to the lower part of the abdomen, the lumbosacral region, both hips and legs. Cautery was used three months before admission on the cervix and uterus followed by deep roentgen-ray therapy without relief of symptoms. For three months she had had difficulty in starting urine and considerable dysuria. Morphine in large doses had failed to give relief, so chordotomy was advised.

A neurologic examination was essentially negative. Physical examination showed nothing pertinent except the large ulcerating carcinoma of the cervix with pelvic metastases.

May 2, 1924, a laminectomy was performed, with removal of the posterior spinous processes and the laminae of the fourth, fifth and sixth dorsal vertebrae. The anterolateral tracts were divided at the level of the seventh dorsal segment to a depth of 3 mm. The incision commenced just in front of the dentate ligament and extended to the emergence of an anterior root.

The laminectomy incision healed promptly. The patient was completely relieved of the pain in the abdomen, back and legs and required no more morphine. On one occasion she complained of pain in the legs but this was not severe and lasted only a short time. Catheterization was not necessary.

A neurologic examination showed no loss in the motion of the extremities. The knee and Achilles tendon jerks were normal. Plantar irritation resulted in flexion of the toes. Tactile, vibratory, motion and position senses were normal. There was loss of pain on both sides below a line 2 inches (5 cm.) below the umbilicus (approximately the eleventh dorsal segment). The temperature sense was impaired from the umbilicus to the groin, below which level it was lost on both sides.

The level of complete temperature loss was much lower than of lost pain sensation although the area of diminished thermal sense, in which the patient was occasionally able to distinguish temperature changes correctly, extended to a higher level than the analgesia. This must indicate in this patient a wider overlapping of the thermal sense in the skin, or a much lengthened crossing in the cord.

CASE 16.—Mrs. A. M., aged 58, had pain due to spasmodic contractions of the legs; a bilateral chordotomy was performed.

About four years before admission she developed sudden cramplike pains in the left hip while walking. The leg would draw up causing her to fall. The pain appeared only at long intervals until two years before admission when it occurred almost daily, especially after she relaxed in a recumbent position. The pain gradually increased in severity and frequency, confining her to bed for the last twenty months. For the last year, the right leg had been similarly involved. During the attacks of pain there was forceful, involuntary flexion of the thighs on the abdomen, of the legs at the knees, and of the toes. The pain always radiated from the hips down the posterior aspect of the legs to the heels.

Physical examination was negative except for marked contractures of the legs, the thighs and knees being flexed. Neurologic and spinal fluid examinations were negative. Roentgen-ray examination was negative except for some arthritis of the spine. The pain was so severe that she cried out during attacks. Morphine had been freely used but only partially alleviated her suffering. No cause for the spasmodic contractions and the pain was ever determined. A bilateral chordotomy was finally advised.

Aug. 13, 1924, a laminectomy was performed, with removal of the posterior spinous processes and the laminae of the fourth and fifth dorsal vertebrae. A bilateral section of the anterolateral columns was made to a depth of 3 mm., the incision extending from the dentate ligaments anteriorly into the anterior roots.

Immediate postoperative recovery was delayed because of a pulmonary complication. The day after operation, she said that her legs felt numb. No change was actually noted in the tactile sensation, however, and this subjective sensation had disappeared the next day. Morphine was discontinued. She had to be catheterized until September 10, when she voided normally. She felt no pain in the legs after the operation.

A neurologic examination, August 29, showed loss of the pain sensation below the ninth dorsal segment on the right and the eleventh segment on the left. Temperature was lost below the crest of the ilium on each side. There was an area of diminished sensation to pin point pain on the inner side of the thigh and in the upper gluteal region on the left (figs. 15 and 16). The tendon of Achilles tenderness was lost, and there was no change in the light touch, vibration, motion and position senses. The reflexes and motion were unchanged, except for a tendency to extension of the great toes on plantar stimulation.

A report a year later stated that there had been no return of pain in the legs although the spasmodic movements still persisted.

CASE 17.—Mrs. A. D., aged 31, had intractable pain due to carcinoma of the uterus; a bilateral chordotomy was performed.

The patient first noted a yellowish, blood streaked, foul vaginal discharge fifteen months before admission. Five months later the cervix was amputated and radium was applied. The carcinoma continued to grow. Later, cauterization was done and deep roentgen-ray therapy instituted without evident benefit. The patient now had extensive metastases and excruciating pain in the lower part of the abdomen and both legs. A neurologic examination was negative.

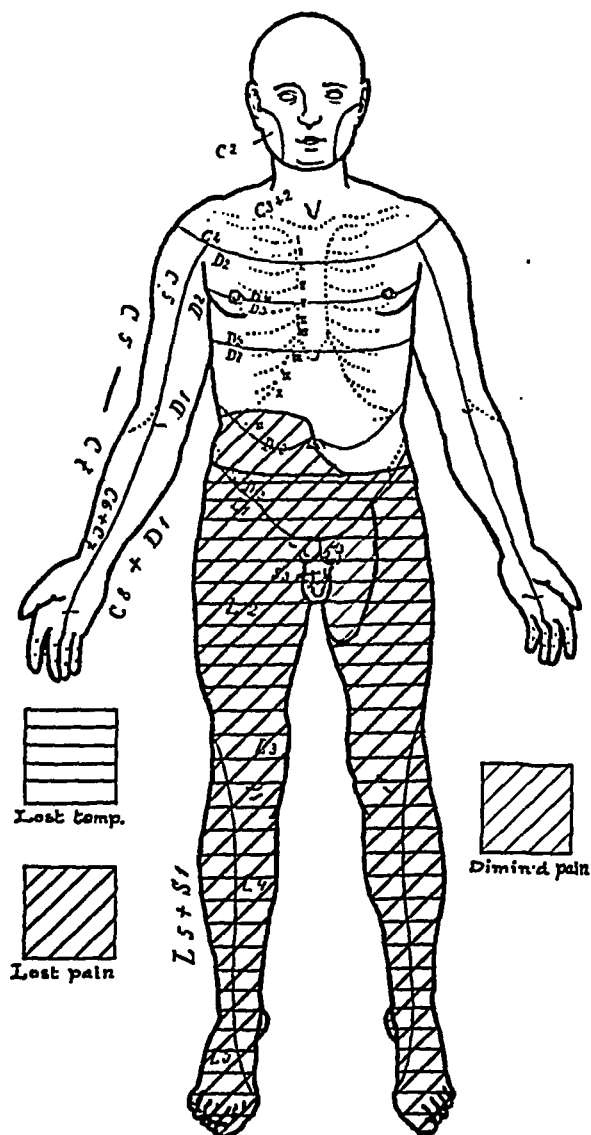


Fig. 15 (case 16).—Areas of lost temperature and pain and diminished pain sixteen days after bilateral section of anterolateral tracts at seventh dorsal segment; incisions were made 3 mm. deep and extended anteriorly into respective anterior roots. Complete relief of pain resulted and no motor weakness. The level of lost pain sensation is higher than that of temperature loss; there is also an area of diminished pain perception on left thigh and right lumbar region.

Dec. 12, 1924, a laminectomy was performed, with removal of the posterior spinous processes and the laminae of the fifth, sixth and seventh dorsal vertebrae. A bilateral chordotomy was done at the level of the fifth spinous process (through

the eighth dorsal segment). The incision, just anterior to the dentate ligament, extended to a depth of 3 mm., circled forward and outward, emerging at an anterior root.

The postoperative convalescence was satisfactory. Catheterization was necessary for the first three days. She was much more comfortable, the chief complaint being pain in the region of the incision. During the day, she was practically completely relieved but nearly every night she required one-fourth grain

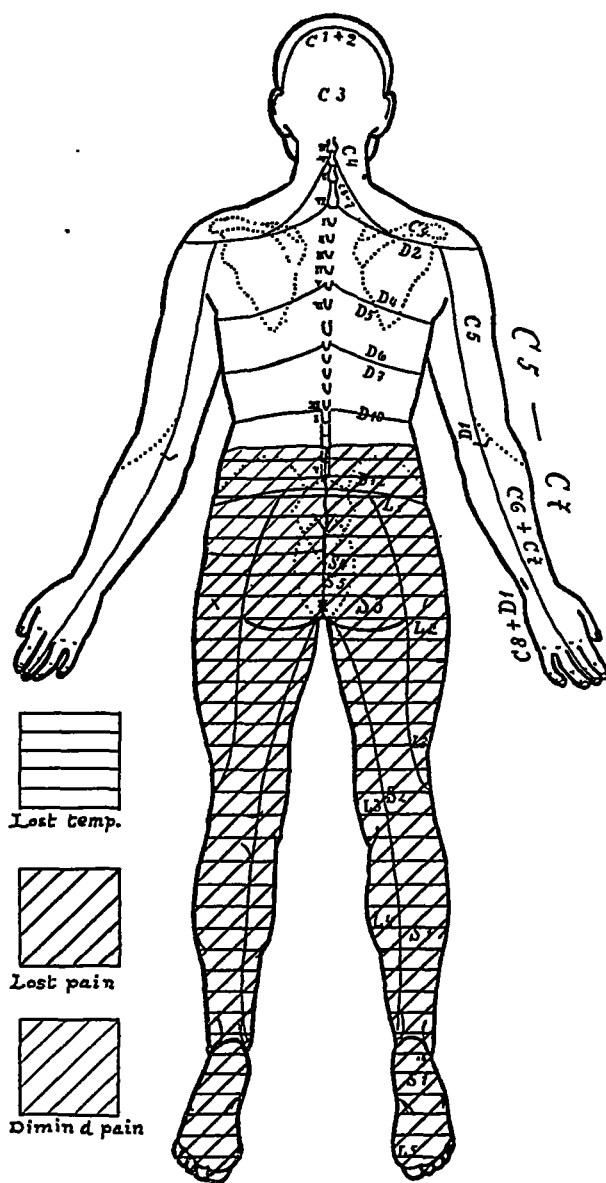


Fig. 16 (case 16).—Back view of patient.

(0.016 Gm.) of morphine, usually for pain in the back and sometimes in the legs. She was much brighter and more cheerful than before operation.

A neurologic examination, December 22, showed normal umbilical, patellar, Achilles and plantar reflexes on both sides; motion, position, vibratory and tactile senses were normal. The temperature sense was not certain up to the groin on each side but was correct in interpretation more often than wrong. A pin point

was not distinguished as such over the anterior and lateral aspects of the right leg and the dorsum of the foot, and a pin point was not felt as painful in many places up to the groin. This loss was not segmented but appeared in irregular areas.

We can offer no explanation for the failure in this case to get a greater loss both of temperature and pain perception. The relief was

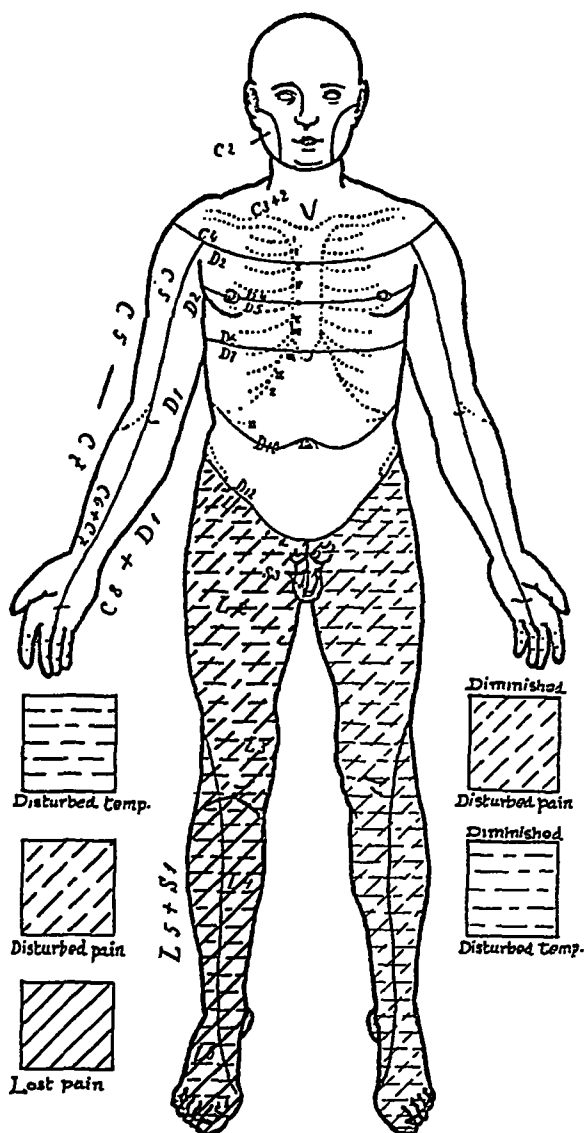


Fig. 17 (case 17).—Areas of temperature and pain ten days after bilateral chordotomy, 3 mm. deep, in eighth dorsal segment; relief of spontaneous pain much greater than area of complete analgesia would indicate; on left, pain and temperature senses were disturbed but not as markedly as on right thigh.

more marked than would be expected from the neurologic findings. This relief, however, was not constant and at times the patient complained of severe pains in the legs.

CASE 18.—Mrs. B. W., aged 35, had pain in the abdomen, lower back, rectum and legs, for which a chordotomy was done.

For the last three months she had had constant, severe, aching pains in the back, rectum, across the lower part of the abdomen and down both legs to the knees. In January, 1923, amputation of the cervix was done; in January, 1924, hysterectomy; in August, 1924, actual cautery to a growth in the upper part of the vagina; in November, 1924, radium therapy in the vagina, and in December, 1924, deep roentgen-ray therapy. The diagnosis was carcinoma of the cervix with

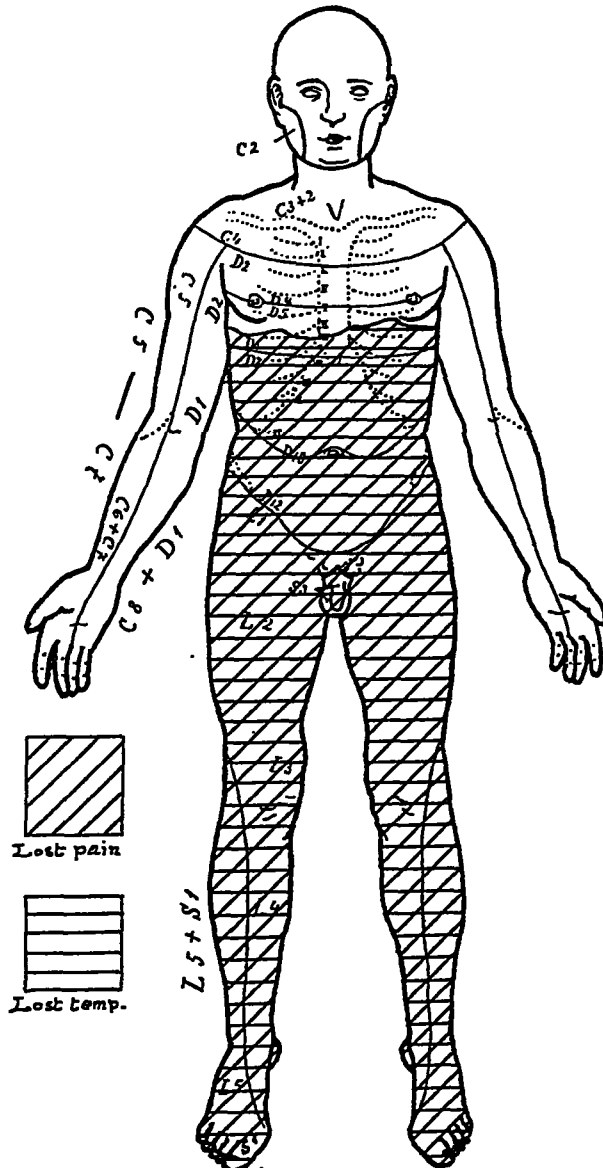


Fig. 18 (case 18).—Areas of lost pain and temperature five days after bilateral chordotomy between fifth and sixth dorsal segments; section of each anterolateral tract to a depth of 3 mm. at dentate ligament and anteriorly through to the mesial side of the exit of an anterior root, which gave the highest level of analgesia and thermanesthesia obtained in any case; no change in motor function, tactile, vibratory, motion, position and deep pressure sensations or in cutaneous and tendon reflexes; complete relief of pain.

pelvic metastases. Since the radium therapy the patient had had difficulty with urination. The pain was now so severe that sleep was not possible even with morphine.

A neurologic examination was negative. A physical examination was negative except for a mass in the pelvis and tight stricture in the vagina. A chordotomy was advised.

Feb. 5, 1925, a laminectomy was performed, with removal of the posterior spinous processes of the third, fourth and fifth and the laminae of the third and

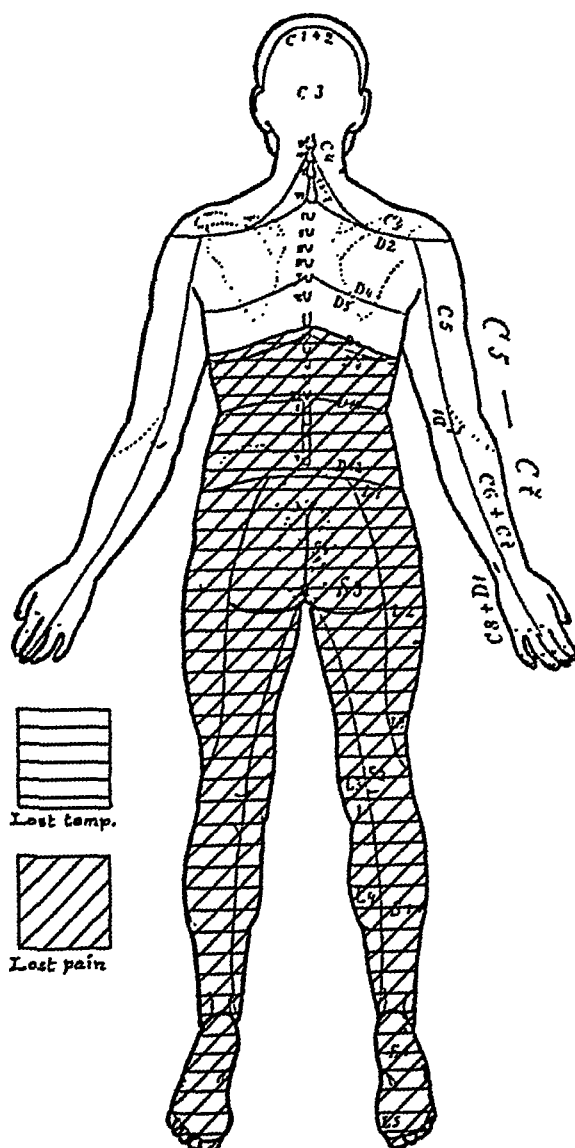


Fig. 19 (case 18).—Back view of patient.

fourth dorsal vertebrae. Section was made of the right anterolateral tract to a depth of 3 mm. at the level of the third posterior spinous process; i. e., the fifth or sixth dorsal segment. The incision was started close to the anterior surface of the dentate ligament and carried anteriorly through the emergence of an anterior root. As a rule, we have not carried the incision quite as far medially, the knife usually emerging at the lateral rather than the mesial side of the motor root. A similar division of the left anterolateral tract was made.

She was completely relieved of pain in the back, pelvis, rectum and legs. Catheterization was not necessary; she was incontinent at times. Morphine was gradually withdrawn and discontinued entirely after the fifth day although she had required large doses before the operation.

A neurologic examination, Feb. 10, 1925, showed all motion in the lower extremities to be normal. The patellar and Achilles tendon reflexes were normal. Plantar irritation caused flexion on the toes on both sides. The vibratory sense was present at the ankles, the tibiae and the patellar and iliac crests. The senses

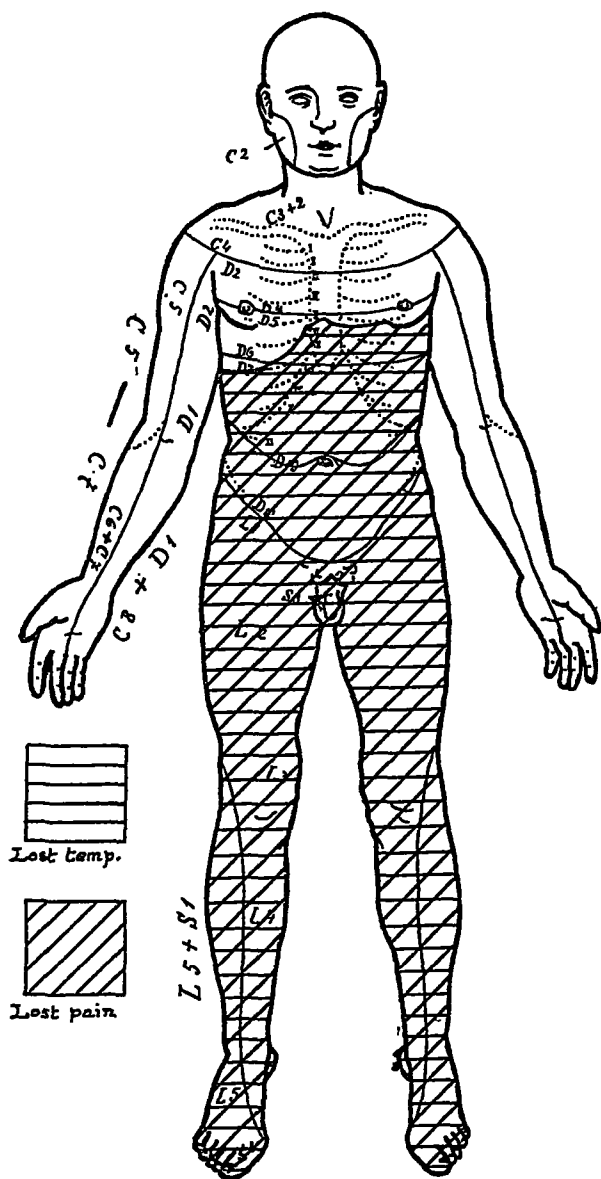


Fig. 20 (case 18).—Areas of lost temperature and pain twenty-nine days after bilateral chordotomy, showing lower level of analgesia and thermanesthesia than was present five days after operation, as shown by figures 18 and 19.

of motion and position were normal. Deep pressure was felt as such, but continued pressure caused no pain. The tendon of Achilles tenderness was lost. The tactile sense was normal. The pain and temperature senses were lost on both sides below a line approximately halfway between the areas supplied by the fifth and sixth dorsal segments (figs. 18 and 19).

A neurologic examination, March 24, showed loss of the umbilical reflex. The patellar and Achilles tendon reflexes were normal. Plantar irritation caused flexion of the toes on both sides. The tactile sensation was normal in the trunk and lower extremities. The senses of vibration, motion and position were normal. The pain and temperature senses were lost on the left side below the fifth dorsal segment (a trifle higher than on previous examination). On the right, the analgesia and thermanesthesia were slightly lower, having dropped to the seventh dorsal segment (figs. 20 and 21).

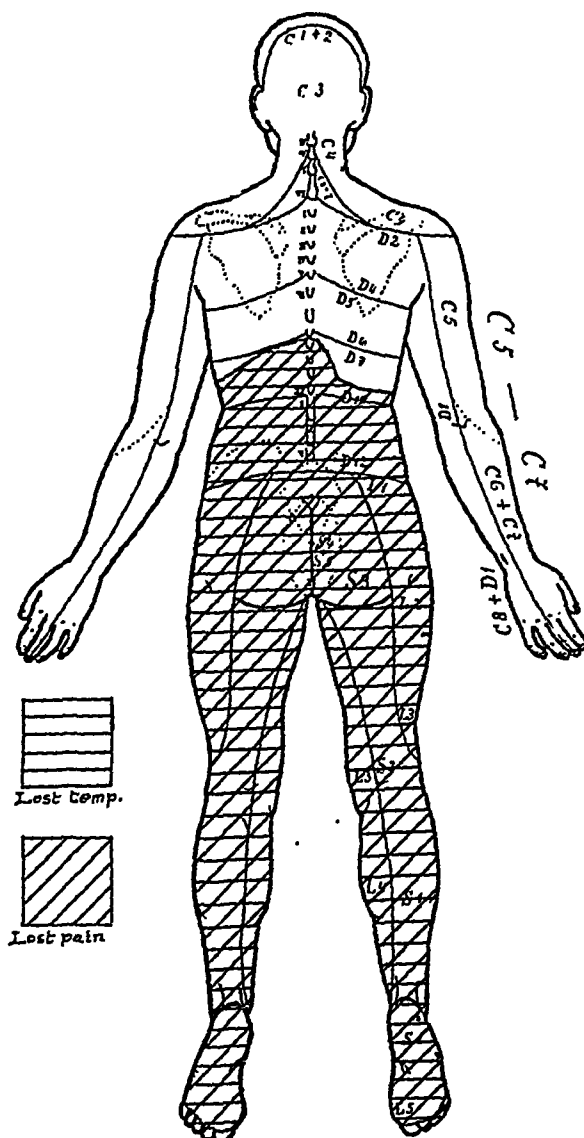


Fig. 21 (case 18).—Back view of patient.

The area of lost pain and temperature sensation extended to a higher level in relation to the anterolateral segment divided than in any previous chordotomy. This we believe is due to the incision being carried deeper in the extreme anterior portion of the tract, the section of the cord fibers extending to the median side of the anterior roots. The division of one motor root is of no consequence in the upper dorsal region.

CASE 19.—C. L., a man, aged 65, suffered excruciating pain in the legs of unknown etiology; a bilateral chordotomy was done.

In January, 1925, he first noticed a "numb" feeling over the entire body, following exposure to cold while digging a well with his feet in ice water. He shortly developed sharp, intermittent pains in the thighs and lower part of the abdomen. Catheterization was necessary the next day, but not since. The inter-

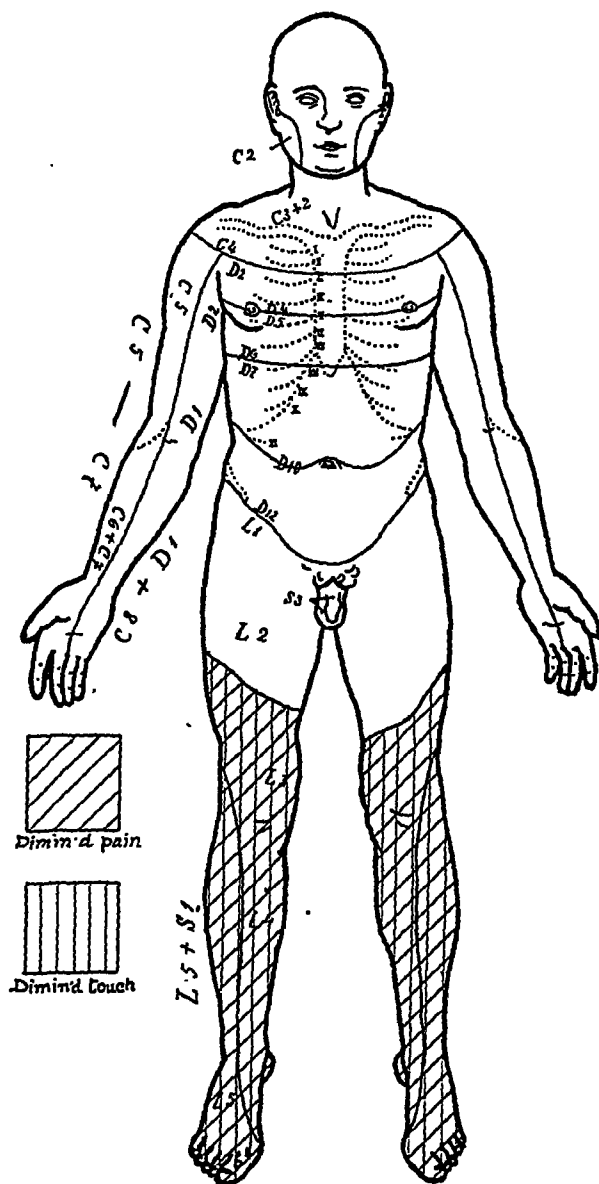


Fig. 22 (case 19).—Areas of diminished pain and tactile perception before operation.

mittent pains, radiating down both legs, but most severe in the left, had persisted. He had some involuntary jerking of the left leg and foot from the onset of the trouble. This had now extended to the right leg and foot. The contractions of the adductor of the left thigh and extensors and flexors of the toes were most marked. These jerking movements were very painful. He had polydipsia and polyuria. The urine examination was negative.

Physical and neurologic examinations, March 20, 1925, were negative except that the plantar reflex was lost in both feet; the tendon of Achilles tenderness was lost, and there was a considerable tremor of both legs when he was standing in the Romberg position. There were coarse, quite rhythmical movements of both lower extremities combined with occasional spasmodic contractions. The patellar reflexes were very active, especially the left. Pin point and light touch

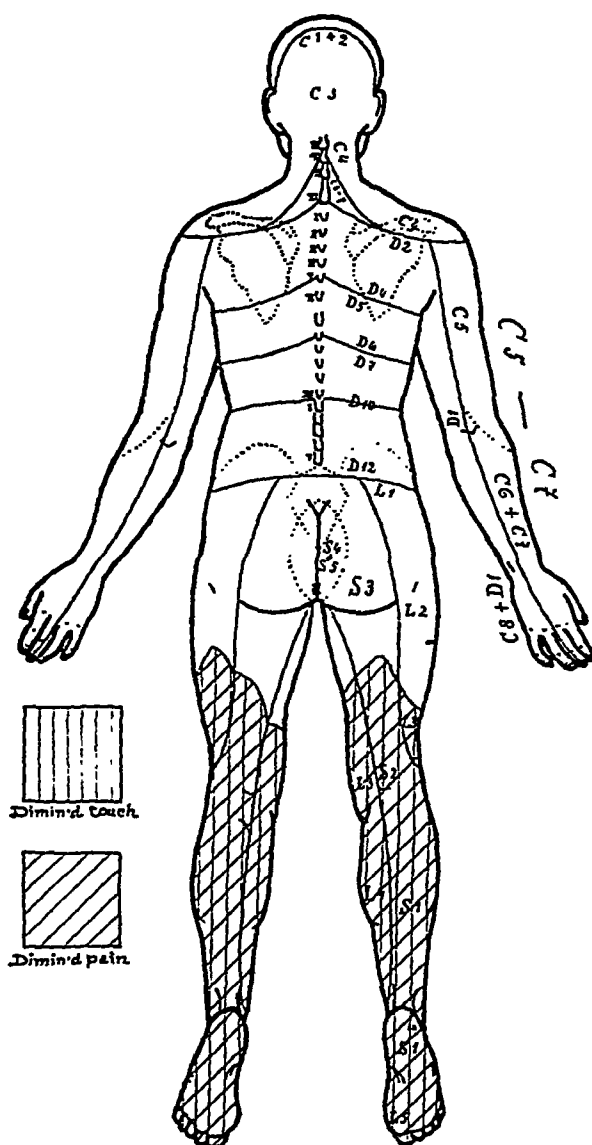


Fig. 23 (case 19).—Back view of patient.

sensations were diminished below the lower third of the thigh in front and the middle of the thigh behind (figs. 22 and 23). The spinal fluid was negative to the Wassermann test, clear, colorless, and gave moderate clouding to phenol. In phase 1 of the Nonne-Apelt reaction there was a faint ring; in phase 2, slight opalescence. The colloidal gold curve was 00122210000; mastic, 222100.

On examination, June 8, the patient complained of severe pain and jerking of the legs and feet, with much pain in the soles of the feet. He had a tingling and

burning sensation in the legs and feet. The Achilles reflex was now lost on both sides. Sensation was the same as before. The vibratory, motion and position senses were normal.

A month later he returned, complaining bitterly of the sharp, shooting pains which now extended downward from the inguinal region on both sides. There also was severe burning along the fibular surfaces and feet. The patellar reflexes

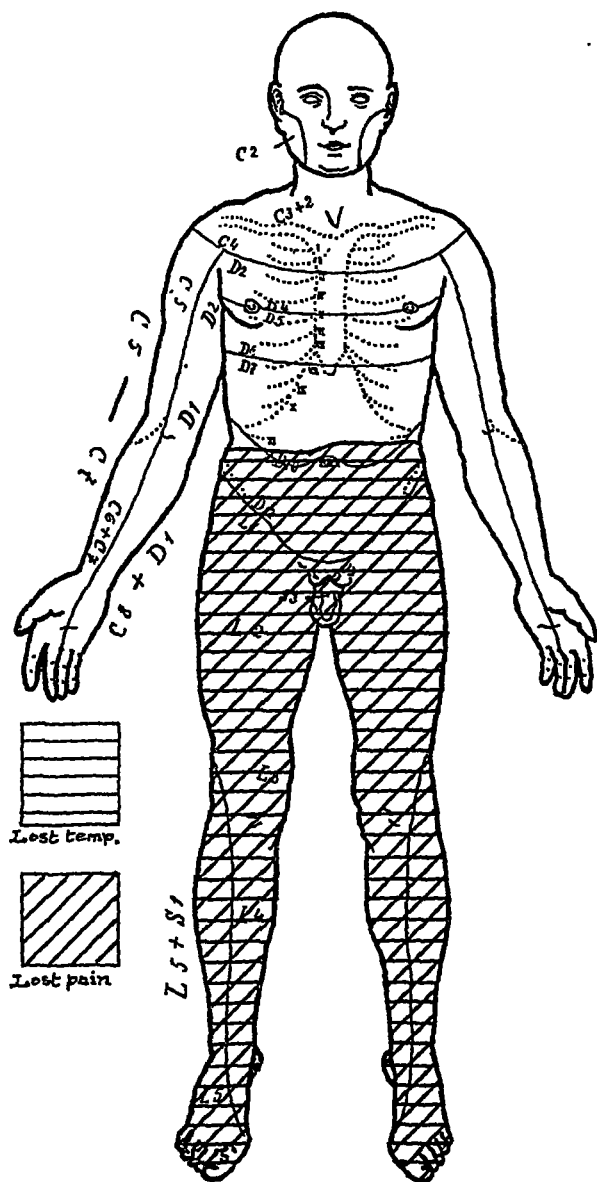


Fig. 24 (case 19).—Areas of lost temperature and pain seventeen days after bilateral chordotomy at eighth dorsal segment; section of each anterolateral tract to a depth of 3 mm. in front of dentate ligament and forward through respective anterior roots.

were normal. The Achilles tendon and plantar reflexes were lost. The light touch sense in the lower extremities had now returned to normal. Pin point pain was still markedly diminished in the same area as before. The tendon of Achilles tenderness was lost. Motion, position and vibratory senses were normal. The thermal sense probably was normal but discrimination was not always accurate.

A definite diagnosis could not be made. Some of the symptoms suggested a tumor or inflammatory condition in the cauda equina. The pain was so severe that exploration even with the very doubtful diagnosis was considered advisable.

July 23, the posterior spinous processes and the laminae of the tenth, eleventh and twelfth dorsal and first and second lumbar vertebrae were removed. No evidence of a pathologic condition could be found. The relief of pain to be

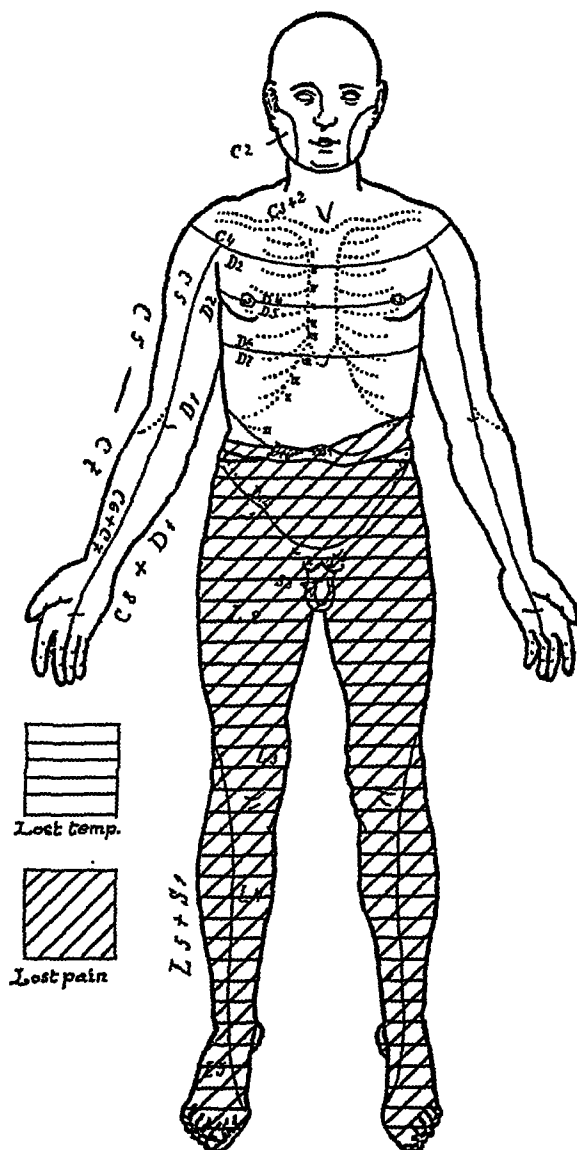


Fig. 25 (case 19).—Areas of lost temperature and pain more than five months after bilateral section of anterolateral tracts at eighth dorsal segment; the level of analgesia and thermanesthesia has remained practically the same.

obtained by a chordotomy at this level was not known, but seemed worth determining. Bilateral division of the anterolateral tracts was made to a depth of 3 mm. at the second lumbar segment. As the motor roots at this level are important, the section of the cord on each side extended only from in front of the dentate ligament to the respective anterior root.

The pain was entirely relieved in the feet, but no change in the pain sensation was noted elsewhere. Accordingly, section of the anterolateral tracts in the usual upper dorsal region was recommended.

August 15, the posterior spinous processes and the laminae of the fourth, fifth and sixth dorsal vertebrae were removed, and a bilateral chordotomy at the level of the fifth dorsal vertebra (eighth dorsal segment) was done. The antero-

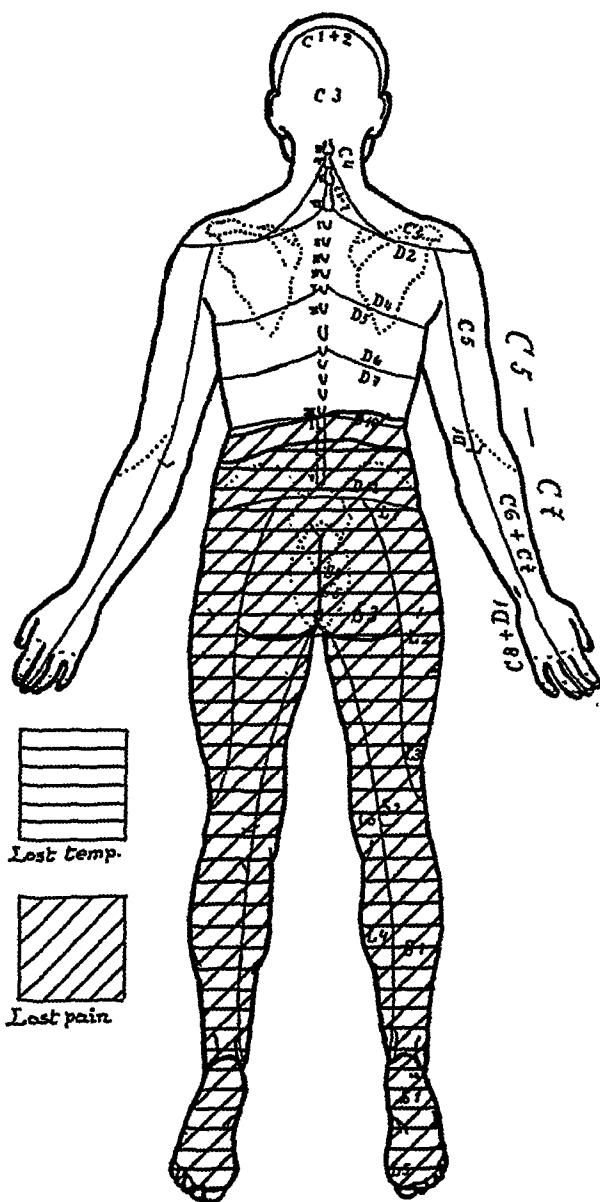


Fig. 26 (case 19).—Back view of patient.

lateral tracts were divided to a depth of 3 mm. just anterior to the dentate ligament. The incisions were then carried forward through the anterior roots on each side.

The severe shooting pains in the legs were completely relieved. The bladder had to be emptied by suprapubic pressure. A neurologic examination by Dr. W. A. Smith, Aug. 1, 1925, showed involuntary twitches of the feet and legs still present. The patellar reflexes were normal. The tendon of Achilles and

plantar reflexes were lost, and the tendon of Achilles tenderness was lost. The vibratory sense was present in the ankles. The pain sense was lost below the level of the umbilicus on the right and to about 2 inches (5 cm.) above the umbilicus on the left. A neurologic examination by Dr. John L. Garvey, September 7, revealed that the patient complained of no pain in the lower extremities but now had a sensation of needles touching but causing no pain in the legs. He also complained, as before operation, of burning and jerking of the legs. The right patellar reflex was normal, the left diminished, and the Achilles tendon reflex was diminished. The plantar reflex was normal on both sides. The vibratory sense was present. The tendon of Achilles tenderness was lost. The sense of motion and position was normal. The pain sensation was lost to the umbilicus on the right, to just below the umbilicus on the left (fig. 24). There was no motor paralysis but the patient would not try to walk, going about in a wheel chair. Shortly thereafter he was persuaded to walk.

The patient returned to the hospital, Jan. 21, 1926. He had had no return of the former pain in the legs but had had sharp, intermittent pains in the chest, the abdomen, the shoulders and the upper part of the arms. He still had burning in the legs, most severe on the left. On the right, only the posterior aspect from the middle of the thigh down was involved. He had jerking of the feet and toes when recumbent but not when sitting or standing, and had incontinence of urine. He now used crutches because the "knees gave way." On neurologic examination, Jan. 25, 1926, the umbilical reflexes were not obtained. The patellar reflexes were active and equal; the tendon of Achilles reflexes were present, more prompt on the right. Plantar irritation caused extension of the toes on the right, no movement on the left. The tendon of Achilles tenderness was lost on both sides. The vibratory, motion and position senses were normal. The tactile sense was normal. The pain sense was lost to the level of the umbilicus on the right and to an ascending line 2 inches (5 cm.) above the umbilicus on the left. The temperature sense was lost below a horizontal level just beneath the umbilicus (fig. 26).

A positive diagnosis was not made. The patient, however, was greatly relieved by the loss of the excruciating pain which radiated from the inguinal region down both legs. The presence of a burning sensation in an area in which both pain and temperature sensations are completely lost is difficult to explain. A point of interest was the difference in the levels of analgesia and thermanesthesia, the former being a segment higher on the left and a trifle higher on the right. The reverse has been noted in a previous chordotomy case.

RÉSUMÉ

The series of nineteen cases that appear in the American literature embrace the reports of Martin and Spiller, Beer, Frazier, Leighton, and Frazier and Spiller. The operation has also been performed by Elsberg, Ernest Sachs and others in this country but the cases have not been published. The primary conditions in the foregoing series which ultimately made operation for the relief of pain necessary were: primary malignant disease of the spine, three; gunshot injury of the spine, three; tabes dorsalis, three; myelitis, two; carcinoma of the rectum, two; carcinoma of the cecum, one; carcinoma of the uterus, one; carcinoma of the breast, one; sarcoma of the thigh, one; shell wound of the sciatic

advocates the removal of retained urine and avoidance of pain due to back pressure, with its danger of renal infection. He considers it unwise to cease abruptly the use of the catheter when there is residual urine. Cabot¹⁶ contends that the catheter must be used whenever necessary to prevent distention, for the sudden emptying of a distended bladder causes vascular changes that permit infection of the bladder mucosa. Jacobson and Keller¹⁵ likewise contend that the catheter of itself is not always the cause of cystitis but that bacterial infection plus retention, trauma and congestion are all more or less necessary factors. Gibbon,²⁴ on the other hand, and many others insist that catheterization should not be instituted after operation unless necessary for pain due to vesical distention and that other expedients should always be tried primarily in an attempt to have the patient void spontaneously. This seems to be the opinion of the majority of clinical surgeons.

ROUTES OF INVASION

The literature is replete with accounts of experimental work done by many investigators in attempts to determine the route by which the colon bacillus reaches the renal and ureteral tissues. The late trend of opinion in this question leans strongly toward the hematogenous route as being by far the most common one.

When there is a marked degree of obstruction with its resulting vascular changes due to malposition of the kidney, calculus, neoplasm or enlarged prostate, an ascending infection along the ureter may occur, possibly in association with a hematogenous or lymphogenous transfer of the infecting organisms. The possibility of bacteria reaching the kidneys by direct extension or continuity must also be borne in mind. Clark²⁵ observed that the bladder in women is rendered especially vulnerable to an adjacent pathologic condition by the intimate anatomic relation of the surrounding genitalia. Furniss¹⁴ cites Bauersein, who found cystitis at eighteen necropsies following operations for carcinoma but no evidence of the infection extending through the bladder wall. Bauersein considered the urethra or the hematogenously infected kidney as the source of infection and held that the operative wound was the portal of entry in more of these cases than is generally believed. Cabot and Crabtree²⁶ assert that colon bacillus infections are usually hematoge-

24. Gibbon, J. H.: *Ochsner's Surgical Diagnosis and Treatment*, Philadelphia, Lea & Febiger, 1:139, 1920.

25. Clark, J. G.: *The Relationship Between the Urinary System and Disease of the Female Pelvic Organs*, Surg., Gynec. & Obst. 18:10 (Jan.) 1914.

26. Cabot, H., and Crabtree, E. G.: *A Classification of Renal Infections with Particular Reference to Treatment*, Boston M. & S. J. 174:780 (June) 1916.

nous in origin and maintain that *Bacilli coli* circulate in the blood under many conditions, being excreted by the kidneys without producing gross lesions. Crabtree²⁷ obtained colon bacillus from the blood in 40 per cent. of thirty-two cases of acute pyelitis. Hess² concluded that infection may ascend by the lumen of the ureter and its lymphatics. He injected virulent cultures of *Bacillus coli* into the bladder of rabbits, with and without previous irritation, and into the pelvis of the kidney, with and without obstruction of the ureter. This same investigator, however, seems to believe the hematogenous route to be the most common one for he injected *Bacillus coli* into the ear vein of animals and was able to follow the bacterial masses from capsule spaces of glomeruli into efferent tubules within a short time (twenty hours) even when there was no evidence of microscopic changes or hemorrhage. Within a few days thereafter no bacteria could be seen in kidney sections, possibly because they were rapidly eliminated. The changes in both kidneys were identical and the renal lesions almost the same as in ascending infection. As regards the transfer of *Bacillus coli* from the colon to the right kidney via the lymphatics, he contends that the lymph glands normally prevent distribution of micro-organisms.

Barber and Draper²⁸ found that, given an infected bladder and making due allowance for local and systemic resistance, the ureterovesical valves may be cut without resulting infection, and showed that the degree of protection afforded by these structures was probably overestimated. At the same time, they found that the kidneys were protected from urogenous infection and hydropic degeneration by the peristaltic action of the ureter.

INCIDENCE AND SIGNIFICANCE OF COLONBACILLURIA AFTER OPERATION

In 1909 Rogers²⁹ of Calcutta recorded a series of eight gynecologic patients who had been operated on and in whom an acute febrile condition had developed as a postoperative complication. The colon bacillus was isolated from the urine in every case and he attributed the disturbed convalescence to urinary tract infection.

In 1911 Williams and Wallace²⁹ of Liverpool, noting Roger's experience, decided they would undertake to determine the incidence of

27. Cabot, H., and Crabtree, E. G.: Etiology and Pathology of Nontuberculous Renal Infections, Surg., Gynec. & Obst. 33:495 (Nov.) 1916.

28. Rogers, L.: Genito-Urinary B. Coli Infections as a Frequent Cause of Fever, Therapist 20:1-4, 1915.

29. Williams, R. L., and Wallace, A. J.: The Incidence, Characters and Significance of B. Coli in the Urine of Gynecological Patients Before and After Operation, Liverpool M. Chir. J. 31:95, 1911.

Bacillus coli in the urine of gynecologic patients and any correlation between postoperative rises of temperature and the presence of this organism in the urine. Colon bacillus was found in 44.5 per cent. of cases before operation and in 93 per cent. after operation, with an appreciable increase in the number of colonies in all postoperative cases. The urine from two cases was sterile throughout and one case with sterile urine showed the highest temperature rise of any in the series. Four other cases were tested after operation only, and a growth obtained in each. There was no marked temperature rise in any case with colonbacilluria. Their conclusions were, in part, that the presence of *Bacillus coli* in the urine of these patients was of little importance and they suggested the use of agglutination tests when there is evidence in the urine of inflammatory changes coincident with colonbacilluria.

Rawls,³⁰ in his study of bacilluria in forty gynecologic cases, found *Bacillus coli* in 20 per cent. before, and 27.5 per cent. after, operation, with more extensive growths after operation. Only one patient in his series had symptoms of urinary infection. The other cases did not present objective or subjective evidence of the absence or presence of bacilluria. He observed that the colon bacillus, as found in gynecologic and obstetric patients, was most often a saprophyte becoming pathogenic when conditions were ripe, such as those which follow obstruction and unanatomic relations.

What then, are the most essential elements in a diagnosis of infection of the urinary tract due to the colon bacillus? Cabot and Crabtree²⁷ consider the following factors necessary: (a) suggestive clinical evidence; (b) bacilli in large numbers in the urine; (c) a trace of albumin, also red blood corpuscles and leukocytes in the urine, and (d) renal function below normal.

METHODS AND RESULTS IN EXPERIMENTAL WORK

During the last year I have made a study of colonbacilluria³¹ in the surgical service of Dr. Carl R. Steinke at the City Hospital of Akron.

30. Rawls, R. M.: B. Coli Infections as a Complication in Gynecology and Obstetrics, Tr. Am. Gynec. Soc. 40:475, 1915.

31. I wish to mention the uniformly satisfactory results which may be obtained by the use of the so-called Greiss test, as a time saving measure for the detection of bacterial activity in urine which has recently been secreted by the kidneys. In 18 out of 20 cases in which the modified Greiss test indicated bacterial activity in the kidneys, the results were confirmed by cultures. This procedure should be of some value, I believe, to the laboratorian and clinician when renal specimens have been collected for culture by catheterization of the ureters. Weltmann, Oskar: Wien. klin. Wchnschr. 35:688 (Aug. 10) 1922.

Urine was collected,³² using care to avoid contamination, and forwarded to the laboratory in sterile test tubes a few hours before operation and from four to six days after operation. The catheter was used to collect all specimens except in a certain number of the male patients. These were allowed to void and the specimen collected after about half the vesical urine had passed through the urethra. The object was to carry on the work under varying conditions in order that the results might be based on ordinary careful hospital routine.

The cases observed were not selected. The 130 patients in this series underwent operations that are representative of those commonly performed in the field of general surgery. The ages ranged from 13 to 71 years, the average being 33 years. The youngest patient in whom a postoperative colonbacilluria was found was 13 years, the oldest 60.

There were ninety-four females and thirty-six males in this group. Among the female patients twenty-four, or 25.5 per cent., had colon bacilli in the urine before, and thirty-eight, or 40.4 per cent., after operation. Of the twenty-four who had preoperative colonbacilluria, all but two had postoperative colonbacilluria. Fifty-six, or slightly over half the female patients, were gynecologic. Fifteen, or 26.8 per cent., had

32. Method for Bacterial Diagnosis of Colon Bacilluria:

1. Special precautions must be taken in collection in order to avoid the possibility of contamination with colon bacillus about the genitalia.
2. The urine should be collected in a carefully sterilized receptacle and cultured within a few hours afterward.
3. From 10 to 20 c.c. or more of urine should be transferred with a sterile pipet to a flask containing 100 c.c. or more of plain neutral broth. This culture should be incubated at body temperature. If the contents remain perfectly clear for at least four days it may be safely regarded as a sterile culture. Slight cloudiness is sometimes due to precipitation of urine salts. Smears are negative but 1 c.c. of the culture should be transferred to a slant of agar and incubated forty-eight hours. If no growth appears the culture is sterile. If colon bacilli are present the mediums are likely to become cloudy within forty-eight hours and should be examined as follows: (a) A stained smear shows short gram-negative bacilli. If other organisms are present it will be necessary to plate out the culture to isolate the bacilli. For this purpose plain agar plates may be used but plates of Endo medium are to be preferred because on these colon bacilli produce a bright red colony. A short gram-negative bacillus is suggestive of the colon bacilli, but before it can be definitely regarded as such it must (1) be motile (usually sluggish); (2) coagulate milk; (3) produce acid and gas when placed in a fermentation tube containing litmus-glucose bouillon; (4) produces acid and gas when inoculated on a slant of Russell's double sugar agar, and (5) produces indol (some strains produce only small amounts).

attempt at this time to isolate and study the many other different organisms that may be found in the urine when cultures are not absolutely sterile.

SUMMARY AND CONCLUSIONS

An attempt was made to determine the importance of laboratory reports that show *Bacillus coli* in the urine of patients following operation.

An unselected series of 130 general surgical cases was studied to determine by culture the incidence and significance of postoperative colonbacilluria.

1. The colon bacillus appears in the urine of a certain percentage of male and female patients who present themselves for surgical operation. The same organism appears in an appreciably larger percentage after operation, often without subjective or objective symptoms of a urinary tract infection.

2. Among female surgical patients of this series colonbacilluria was present from three to five times more often than among male surgical patients.

3. Colon bacilli occurring in the urine in abundance after operation is a presumptive sign of urinary tract infection, but in the absence of other confirmatory evidence does not always account for postoperative complications.

4. Gynecologic cases, as a class, have colon bacilli present in the urine after operation probably more often than any other class of surgical subjects.

159 South Main Street.

SPONTANEOUS DISLOCATION OF THE TENDON OF THE LONG HEAD OF THE BICEPS BRACHII

REPORT OF FOUR CASES *

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PALO ALTO, CALIF.

I have used the word spontaneous advisedly in order to convey the idea that external trauma, accident or disease is not necessarily involved in the cases I have observed. These dislocations were uncomplicated in the customary sense but not acutally so, because they were all associated with destruction of portions of the articular capsule by use. This, to be sure, is a traumatic destruction but not in the usual sense, for the trauma concerned was not due to external causes but resulted from use of the extremity.

Dislocation of the tendon of the long head of the biceps brachii, uncomplicated by the dislocation of the joint or by external trauma, remains an almost unrecorded and also a disputed thing. After a review of the literature, White¹ in 1884 came to the conclusion that the case observed by him probably was the only genuine one up to that time.

Since 1884 the Index Medicus lists only a single article on this topic, by Robinson² in 1902. Robinson diagnosed and demonstrated his case as one of "dislocation of the tendon of the long head of the biceps flexor cubiti," but later reported that "the case shown under the above title did not prove so on operation. The biceps tendon seemed securely held in its groove, but there was a very thickened bursa over the great tuberosity, in relation with the insertion of the supraspinatus. The tuberosity itself was irregular and thickened evidently owing to osteoarthritis." The existence of a greatly thickened supratubercular or subdeltoid bursa in this case is of especial interest to me, because in the many hundreds of cases of use-destruction I never have encountered such a case.

Only a few works on anatomy and surgery mention dislocation of the tendon of the long head of the biceps among surgical lesions. Treves³ (undated), for example, merely stated that "in certain violent wrenches of the limb the tendon may slip from its groove and be dis-

* From the department of anatomy, Stanford University School of Medicine.

1. White, J. W.: A Case of Supposed Dislocation of the Tendon of the Long Head of the Biceps Muscle, *Am. J. M. Sc.* 87, 1884.

2. Robinson, H. B.: Dislocation of the Long Tendon of the Biceps Flexor Cubiti, *Tr. Clin. Soc. London* 36, 1902-1903.

3. Treves, Frederick: *Surgical Applied Anatomy*, Philadelphia (about 1883).

placed to one or the other side, usually the inner side." The idea that sudden exertion can dislocate the normal tendon is common but probably erroneous.

Davis ⁴ in 1907, writing in Piersol's *Anatomy*, declared that "inward dislocation of the tendon of the long head of the biceps muscle has probably occurred from direct violence as an uncomplicated lesion in a few cases." Since a dislocation of the tendon from "direct violence" would undoubtedly have to be complicated by other injuries to skin and muscles, I presume that what Davis really meant was that the dislocation of the tendon may be uncomplicated by dislocation at the shoulder.

In his *Applied Anatomy*, Davis ⁵ in 1910 wrote: "This tendon is comparatively rarely luxated, because it is firmly held in place by the transverse humeral ligament. . . . Luxation of the tendon outwardly would be opposed by the insertion of the pectoralis major; therefore it is only displaced inwardly." It seems to follow from this that Davis merely had dislocation of the distal portion of the tendon in mind, for luxation of the proximal portion could not be prevented by the tendon of the pectoralis major.

Under the head "Dislocation of Muscles and Tendons," Da Costa ⁶ in 1915 stated that "the tendon of the biceps is oftenest displaced," without specifying, however, which biceps tendon is so affected. Da Costa added that the tendon of the flexor carpi ulnaris, peroneus brevis, peroneus longus, tibialis posticus, sartorius and even that of the plantaris may be dislocated. He stated, however, that fracture or chronic arthritis are usually responsible for these dislocations and added that "displacements may exist after a solitary injury. . . . Dislocation of the long head of the biceps may occur laterally early in the progress of rheumatoid arthritis of the shoulder joint, and the displaced tendon may be absorbed."

No one will dispute the fact that external violence may dislocate any organ in the human body, but aside from this it is difficult to see how the tendon of the plantaris or some others mentioned by Da Costa could be dislocated by chronic arthritis. I have seen many effects of severe chronic arthritis in the dissecting room, including marked destruction in the shoulder and other joints, but I have never seen a case of lateral dislocation of the tendon of the long head of the biceps, and on anatomic grounds I doubt whether lateral displacement ever occurs except from external forces that first destroy the tendon of the supraspinatus and joint capsule.

4. Davis, G. G.: *Human Anatomy*, Philadelphia, Piersol, 1907.

5. Davis, G. G.: *Applied Anatomy*, Philadelphia, 1910.

6. Da Costa, J. C.: *Modern Surgery, General and Operative*, Ed. 2, Philadelphia, 1919.

Binnie⁷ in 1907, writing on the surgery of muscles, tendons and bursae, stated that "luxation of the tendon of the biceps has been described. It is difficult to imagine this injury occurring without dislocation or fracture of the head of the humerus." This conclusion of Binnie confirms the opinions of Volkmann and Chassaignac as quoted by White. In Binnie's "Treatise of Regional Surgery" in 1917, Frick⁸ spoke only of displacement of the tendons of the peroneus longus and the "tibialis anticus and posticus."

Under the paragraphic caption "slipping of the long head of the biceps" Estes⁹ in 1922 stated that "a loose position of this tendinous part of the biceps occasionally causes disability and can be remedied by severing the attachment near the head of the humerus and thus throwing it out of action." As an anatomist largely unfamiliar with surgical procedure I cannot help but express my surprise at the naive and heroic treatment suggested for the alleged condition.

Steindler¹⁰ in 1923 stated:

The biceps tendon often is displaced from its bed in the sulcus intertubercularis and in the majority of cases only a few strands are left of the intra-articular portion of the tendon, since the rupture occurs very near to the place of origin at the upper margin of the glenoid cavity. Often the upper extra-articular portion of the tendon is adherent to the sulcus intertubercularis, being caught at times under a bony ridge.

I am not at all certain as to the meaning of this paragraph but it would seem that the author had in mind only conditions following rupture of the tendon.

I surmise that the statements of Davis and Da Costa are based largely on the article of White. After a comprehensive review of the literature, White concluded that the cases previously reported "fail altogether to carry conviction, the one case which possesses any strong element of probability being itself open to reasonable doubt." The case referred to by White is that of Soden. In this case the tendon of the long head of the biceps brachii was supposed to have been dislocated by a fall on the elbow which forced the humerus upward against the acromion. Unexpected and strange results, no doubt, often follow accidents, yet it seems unlikely that this tendon could be thus dislocated without other injury to the joint. It would be forced more firmly into

7. Binnie, J. F.: *Surgery of the Muscles, Tendons and Bursae*, in Keen, W. W.: *Surgery, Its Principles and Practice*, Philadelphia, 1907, 2.

8. Frick, W. J.: *Traumata of the Lower Extremity: A Treatise on Regional Surgery* 3, Philadelphia, 1917.

9. Estes, W. L.: *Deformities of the Shoulder*, in Ochsner, A. J.: *Surgical Diagnosis and Treatment* 4, Philadelphia, 1922.

10. Steindler, Arthur: *Reconstruction Surgery of the Upper Extremity*, in *Surgical Monographs*, New York, Lewis, Pool and Elting, 1923.

the sulcus by an upward displacement of the humerus, if such were possible without fracture of the acromion. It is much more likely that Soden's case was one in which the tendon had been dislocated before the occurrence of the foregoing accident, that is, that it was similar to those here reported and that the accident only revealed the condition.

After a review of the literature and a four page anatomic description of the shoulder in which White used two figures from Gray not true to life and inadvertently not credited, he gave a fourteen page discussion of a case that he had seen as a consultant *three years previously*. Although White's title is "a case of supposed dislocation of the tendon of the long head of the biceps," he nevertheless concluded his discussion with the opinion that it was one of uncomplicated luxation. Unfortunately, however, neither the case nor White's analysis of it compels this conclusion for White erroneously assumed that: (1) Considerable space normally exists between the acromion and the humerus; (2) the tendon of the long head of the biceps depresses the head of the humerus, thus normally maintaining an acromiohumeral interval; (3) the subscapularis necessarily acts more powerfully as a medial rotator after the humerus has been forced against the acromion; (4) pressure from the displaced tendon of the long head of the biceps on the tendon of the subscapularis stimulates the latter muscle to spasmodic contraction; (5) the dislocated tendon of the long head would itself strongly aid medial rotation of the humerus; (6) the supraspinatus is a powerful lateral rotator; (7) the acromion on the affected side was tilted upward by "the presence of the head (of the humerus, A. W. M.) just beneath its tip," and (8) medial dislocation of the tendon of the biceps will put the tendon on the stretch because the distance between the opposite terminal attachments of the muscle is increased under these circumstances.

It seems unnecessary to discuss these misconceptions for their erroneous nature is self-evident. White also believed that he palpated an empty intertubercular sulcus from $1\frac{1}{2}$ to 2 inches (3.7 to 5 cm.) distal to the acromion where the sulcus is shallow and where it lies beneath the deltoid and the broad tendon of the pectoralis major. He also thought that he felt the dislocated tendon itself, but apparently was somewhat in doubt although he mentioned the fact three times. It is to be doubted whether White could feel the sulcus in the location stated, for he reported that the "bursae and capsule" over the region of this groove "were drawn so tightly and were so tense by reason of their connection with the sheath of the tendon that swelling could not occur (the succeeding symptom . . . will explain my reason for thinking that this sheath was put greatly on the stretch, but not lacerated)." It must also be remembered that the patient was a carpenter and that the

deltoid hence probably was well developed, thus adding to the difficulty of palpating sulcus or tendon. However, the most convincing thing against the genuineness of White's case is its assumed genesis. White stated that the dislocation was produced by a fall from a height of 6 or 8 feet in which the right shoulder was struck a glancing blow from above and medially, *but without subsequent ecchymosis except along the region of the intertubercular sulcus*. It is exceedingly doubtful, indeed, that a blunt edge such as that of a piazza floor could gouge the normal tendon of the biceps out of its groove, detach the articular capsule and not seriously injure the deltoid and the overlying skin. When it is recalled how completely the distal portion of this tendon is covered by the retinaculum and how firmly the articular capsule holds it in the groove in the intertubercular region, dislocation of it under such conditions seems wholly inconceivable, in a normal joint. However, as in the case of Soden, it is possible that the tendon of the biceps in this case had been dislocated before the accident or that it was a case in which the tendon had previously been destroyed and had obtained a secondary attachment in the region of the lesser tuberosity. Since this patient also was a carpenter this assumption gains greatly in probability.

As the tendon of the long head, in all cases of its dislocation which have come to my notice, was still in the sulcus in the region in which White thought that he felt it absent, it seems not unlikely that what White took for the displaced tendon of the long head was the tendon of the short head, which is easily palpable.

I realize fully that an anatomist cannot speak with authority on matters of palpation except that he ought to know fairly well whether a structure is located in a region in which it is alleged to be palpable. I cannot refrain from expressing my skepticism regarding the general statement of Da Costa that a dislocated tendon "can be felt and a hollow exists where it normally lies." Think of palpating the tendon of the plantaris. Da Costa further stated that "when the muscle contracts the tendon is felt to slip from its groove." If so, then it surely cannot have been permanently dislocated nor its groove been palpable. Da Costa further held that "when the biceps is dislocated the head of the bone passes forward (so called subluxation of the humerus)." It must be evident that anterior dislocation of the tendon of the long head of the biceps might tend to displace the humeral head posteriorly but not anteriorly. As a matter of fact, however, the humeral head showed no displacement whatever in the four cases of maximal dislocation of the tendon of the long head which I have observed in the dissecting room, and there is no reason to suppose that postmortem restitution took place.

I saw the first of my four cases some years ago. Since then I have observed three more instances of complete dislocation, making a total of four among 286 cadavers, or 1.25 per cent. Of these, 235 were male and fifty-one female cadavers. Only one of the four cases was observed in the body of a woman. All occurred in adults and the ages ranged between 50 and 80 years.

This is an amazingly high incidence for so strange a happening, but I surmise that an earlier recognition of the occurrence of this condition on my part and a closer scrutiny of the dissecting room material, would have revealed additional cases of incipient dislocation at least. It must be remembered, however, that the incidence of this condition in the general population of the same ages undoubtedly is far lower, for a much smaller percentage of them are hewers of wood and drawers of water. Yet the condition undoubtedly is common enough but remains undiagnosed. I myself failed to recognize two other cases discussed in 1924 as cases of relatively early dislocation.¹¹ Reference to Figure 7 in that article will show that the "widening" of the intertubercular sulcus on which I commented really represents a transition stage in the dislocation of the tendons.

It is doubtful whether severe or sudden strain, even if prolonged or repeated, can produce this dislocation. It probably cannot be regarded as an effect of sudden exertion for in all these four cases, months and probably decades, if not years, of prolonged wear and strain undoubtedly were necessary for its production. Probably strenuous and long continued use resulting in capsular defects alone can produce the conditions necessary for its occurrence. I have previously reported that considerable destruction of the superior portion of the articular capsule can exist without evident injury or destruction of the tendon of the long head, and the opposite also is true.¹¹ This fact can be explained only by assuming that the destructive agent is noninflammatory and that the destruction proceeds gradually, for it is only in this way that the parietal layer of the synovial membrane can be destroyed and an unaffected tendon exposed for a considerable extent.

It was not surprising to me that this tendon might be displaced slightly anteriorly while being severed by attrition and before it secured a firm secondary attachment near the lesser tuberosity. But this is quite a different thing from the dislocation of a perfectly intact tendon over an intact lesser tuberosity.

Every anatomist is aware of the varying prominence of the tuberosities and the tubercular crests and hence also of the varying depth of the intertubercular sulcus. But in spite of such variations the tendon

11. Meyer, A. W.: Further Evidences of Attrition in the Human Body. *Am. J. Anat.* 34:241 (Sept.) 1924.

of the long head usually is anchored so securely by the strong capsular attachments that bridge the proximal portion of the sulcus, and by the retinaculum bridging it farther distally, that dislocation of the underlying tendon would seem to be impossible as long as these structures are intact. Sudden contraction of the muscle could not injure them sufficiently to disengage the tendon.

The intertubercular sulcus sometimes even extends over the periphery of the articular cartilage and the tendon is held firmly down in the sulcus by muscular tone and contraction. Moreover, during contraction of the biceps, in the position of medial rotation of the arm, the tendon would be pressed against the anterior surface of the greater tuberosity, not forward against the lesser. As long as the tendon of the long head remained in the sulcus it would hence pass obliquely upward and backward from the proximal portion of the sulcus to its point of origin, in the position of medial rotation of the humerus. Consequently, energetic contraction of it in this position would tend to dislocate it backward, not forward. This, however, would be impossible without detachment of the capsule and the insertion of the supraspinatus.

It is true that the more distal portion of the retinaculum—the transverse humeral ligament—varies considerably in strength, but displacement of the tendon in the more distal portion of the sulcus was slight in these four cases. It practically remained in place here. Sometimes the retinaculum immediately distal to the tuberosities forms a thick tendinous band, which would be unlikely to yield under any conceivable intravital circumstances except external trauma. At other times, however, it is extremely thin and cannot, by itself, be regarded as an important factor in retaining the tendon within the sulcus. But this can be a matter of secondary importance only, for the yielding that must initiate dislocation of this tendon must occur in the intertubercular region at the place of attachment of the articular capsule, which is thickened in this region.

The uninjured tuberosities always form an impassable barrier for the tendon as long as the capsule does not yield. The tendon can only be displaced after being lifted sufficiently to slip over either tuberosity. In the cases I have observed it always was displaced over the lesser tuberosity, never over the greater. The extent to which the tuberosities prevent displacement is, however, determined largely by the position of the brachium. In the position of marked medial rotation the lesser tuberosity ceases to be an obstacle to anterior displacement of the tendon, but unless the latter is relaxed considerably it would be urged against the medial surface of the greater tuberosity under these circumstances, by muscle tone and contraction.

In one of these four cases of dislocation saccular extensions of the articular cavity were contained in the greatly thickened capsule in the

region of the sulcus. These diverticula were about 2 by 0.5 cm. in size and opened by means of narrow necks into the proximal portion of the intertubercular sulcus. Both diverticula had a trabeculated wall and probably were produced by contact of the articular capsule with the coracoid, between which and the tuberosities it had been rolled in every medial rotation of the brachium. That these capsular diverticula probably were formed in this way is suggested by such facts as those reported by me in 1921 and 1924.¹²

In the latter article I stated that two superimposed bursae sometimes are found in the region of the olecranon. I recently have observed a similar condition under the acromion. In addition to the normal subdeltoid or subacromial bursae, an additional small bursa was contained in the connective tissue overlying the periosteum on the under surface of the acromion. This bursa, which was approximately a centimeter in diameter, very evidently had formed in the subacromial connective tissue by contact with the greater tuberosity during abduction. However, the implication is not that there necessarily exists a similar direct contact between the humerus and the coracoid in such cases as those just referred to. That is ordinarily impossible.

The only case in which I have observed polishing of the coracoid was one of cancer *en cuirasse*, referred to in a former paper.¹³ In this case neoplastic infiltration and consequent contraction of the greater pectoral muscles had drawn the humeri forward against the coracoids and resulted in partial destruction of them and of polishing of their surfaces and of the contiguous part of the heads of the humeri. Before this contact was possible the anterior portion of the articular capsule had to be destroyed, to be sure. The same thing applies to the periosteum over the coracoid, the articular cartilage of the humeral head and to the intervening connective tissue. Aside from this case, I have never seen it, and I know of no evidence indicating that contact between the coracoid and the humerus is possible, under normal conditions. I did not find such wear present in humeroscapular articulations in which the entire upper half of the articular capsule had been destroyed by use.

Anterior dislocation of the long head of the biceps must result in relaxation of the tendon for the interval between its two opposite points of attachment is decreased thereby. Hence there must be a reduction in the effectiveness of the contraction of the lateral portion of the muscle. However, it is possible that this relaxation of the tendon may in the

12. Meyer, A. W.: Unrecognized Occupational Destruction of the Tendon of the Long Head of the Biceps Brachii, Arch. Surg. 2:130 (Jan.) 1921; Footnote 11.

13. Meyer, A. W.: Further Observations Upon Use-Destruction in Joints, J. Bone & Joint Surg. 4:491 (July) 1922.

course of time be compensated for by greater contraction of its lateral belly, but it is doubtful whether such an adjustment occurs promptly. Hence the tendon would be more or less relaxed whenever the muscle is not active. It also follows that the shoulder joint must be weakened somewhat through such a displacement of the tendon of the biceps wholly apart from the weakening resulting from a loosening of the articular capsule in the injured region.

Since the migrating tendon presses against the joint capsule in the area of advance, it always lies in a capsular and retinacular sling. Moreover, as soon as it encounters the tendon of the subscapularis, it comes to lie on the latter. Because of these things and its protected position, the dislocated tendon is not subjected to attrition after it has reached its definitive position below and in front of the lesser tuberosity. This would be true, I think, even if it were subjected to the same tension as before, for it would tend to lie in the shortest line between its two attachments and hence remain protected. While it lies on the lesser tuberosity during transition or intermittently after dislocation it might, however, be subjected to decidedly more wear, but it certainly would not be absorbed.

I do not know how much pain and disability may accompany this dislocation, but it is more than likely that more or less discomfort is present and that a person so affected would protect the joint concerned by vicarious use of the other extremity, and thus save the yielding capsule or the displaced tendon.

In each of these four cases of dislocation it was easy to replace the tendon in the sulcus, but I doubt whether it would remain there in the living even if the detached capsule were sewed securely to the underlying bone, unless this procedure were accompanied by a change in occupation which not only made forcible contraction of the biceps unnecessary, but also obviated the movements responsible for the displacement. Surgical intervention, no doubt, would provoke bony proliferation and result in the formation of undesirable adhesions, and merely to sever the tendon seems wholly unjustifiable. It would seem that it should at least be attached in the region of the tuberosities where the spontaneously severed tendon so often becomes adherent.

Marked abduction of the upper extremity would continue to cause buckling of the joint capsule against the acromion as before, and would be accompanied by attrition as before. This, if excessive, would again lead to destruction of the new capsular attachment and to redislocation if not to destruction of it. These, however, are matters for surgeons, and I like to remember the old saying, let not the cobbler go beyond his last.

It must be evident that the shifting of the intact tendon of the long head of the biceps here reported is quite a different thing from the partial destruction of it and of the supraspinatus and subscapularis tendons accompanying some cases of complete destruction of the superior half of the humeroscapular capsule. However, both conditions apparently are due to use. The destruction of the tendon of the iliopsoas sometimes seen in connection with fracture of the neck of the femur with consequent upward displacement of the bone with resulting contact between the lesser trochanter and the tuberosity of the ischium also is due to wear, but not under normal conditions of the joint. I have seen destruction of the latter tendon also in a case of upward displacement of the acetabulum, or rather of a relocation of the acetabulum at a higher level on the ilium. However, these and other similar phenomena are quite different things from the dislocations of the uninjured tendon of the long head of the biceps brachii here under consideration, and only incidentally are occupational in origin.

An examination of several hundred humeri fails to reveal variations in the intertubercular sulcus or in the lesser tuberosity at all adequate to account for this surprising dislocation. Nor do I know of capsular anomalies responsible for it. It is not necessary that attrition against the acromion during abduction should first completely destroy or loosen the articular capsule in the region of the lesser tuberosity before this dislocation can begin, although such destruction was present in three of these four cases. In the other case, lesser attritional defects were present in the capsule only. The lesser tuberosity itself had not been materially affected.

The exact position of the dislocated tendon depends, to be sure, on the degree of displacement which it has undergone. When completely dislocated, that is, when the displacement has been maximum, the tendon extends downward and forward from its scapular attachment at the supraglenoid tubercle and the adjacent fibrocartilage. It lay closely against the anterior portion of the articular capsule in all four cases, and was entirely free from adhesions. It is highly probable that the synovial sheath that is carried forward with it, although greatly widened in the process of dislocation, is largely responsible for the absence of attritional effects on the tendon.

The fact that the tendon was not adherent and wholly preserved, even when the entire superior portion of the articular capsule was completely destroyed, shows conclusively that arthritic processes were not responsible for its dislocation. An arthritis, severe enough to destroy the entire thicker upper half of the articular capsule, and rarely also the tendon of the supraspinatus, certainly would not leave the tendon of the long head of the biceps or the thin inferior portion of the capsule intact. Yet

the latter was invariably the case. I have never seen this portion of the capsule affected in the least, no matter how amazing the destruction in its upper portion or how great the bony changes.

In regard to the genesis of this novel dislocation, it seems to me that it can be produced only after destruction of the superior portion of the articular capsule, and then only in the position of marked abduction and lateral rotation, facilitated, perhaps, by flexion of the forearm in the position of supination. Such conditions would produce a maximal relaxation of the tendon and permit it to be carried forward over the lesser tuberosity. Once dislocated it probably would always remain so, especially if continued attrition in the region of the tuberosities lead to bony proliferation and partial or total obliteration of them and of the inter-tubercular sulcus.

I have not, as yet, reviewed the published cases of rupture of this tendon, nor have I ever seen a case, but am prompted to suggest that weakening by attrition may be an important predisposing, if not an invariable, cause for this accident. It is evident that rupture of this tendon must have occurred in all cases in which I found it divided by friction, and in which it had not previously secured a firm secondary attachment in the region of the lesser tuberosity. Moreover, had any of these patients, or those with dislocation of the tendon here reported, sustained an injury of the shoulder, it would have seemed that this accident had produced the rupture or dislocation instead of merely furnishing circumstances that directed attention to the conditions.

PULMONARY COMPLICATIONS FOLLOWING ANESTHESIA AND OPERATION

A STATISTICAL STUDY *

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AND

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As a rule little consideration is given to the prevalence of respiratory infection in the community as an important factor in the incidence and the etiology of pulmonary complications after anesthesia and operation. An analysis of a series of such cases has impressed us with the importance of infection, especially epidemic respiratory infection, in the causation of these conditions and has prompted this report.

In the surgical division of the Hospital of the University of Pennsylvania during the last thirty-two months a study has been made of these conditions. As soon as a patient, after anesthesia and operation, is suspected of having a respiratory complication by the surgical house officer, a medical consultation is requested and the patient remains under the care of the medical consultant until the complication is terminated. Clinical findings are checked whenever possible by roentgen-ray examinations. On the basis of these observations an attempt has been made to evaluate the relative importance of the various etiologic factors in these conditions.

INCIDENCE

During the period from Sept. 1, 1922, to May 1, 1925, 5,966 operations were performed in the surgical service. This includes the departments of general surgery, neurosurgery and genito-urinary surgery. It does not include the departments of gynecology, obstetrics, otolaryngology, ophthalmology or the surgical outpatient clinic. In the 5,966 operations, sixty-nine respiratory complications after anesthesia occurred, an incidence of 1.15 per cent. An analysis of these complications is shown in table 1.

The diagnoses bronchopneumonia and lobar pneumonia, as is usual, comprise the majority, 61 per cent, in our series. The diagnosis in each instance was that made by the medical consultant and in twenty-nine of the sixty-nine cases was confirmed by roentgen-ray examination or necropsy or both.

* From surgical division B and the medical division of the Hospital of the University of Pennsylvania.

ETIOLOGY

The contributing causes of postanesthetic, postoperative pulmonary complications have often been enumerated. They include a preexisting respiratory infection, acute or subacute, as met with so often in patients for emergency operation, or the various types of chronic respiratory disease, not omitting sinus infections; prolonged anesthesia; undue chilling of the body due to such factors as improper clothing and covering, delay in transport to and from the operating room in drafty hallways, excessive exposure in the operating room during the course of a prolonged operation, and a failure promptly to change moist garments; the aspiration of mucus and septic material; diaphragmatic paralysis following injudicious retraction in operations in the upper part of the abdomen; lung embolism, and finally, massive atelectasis due, according to Chevalier Jackson, to plugging of a main stem bronchus by inspissated mucus and the subsequent absorption of air from the distal lung.

We were interested to note that our sixty-nine cases of respiratory complications fell into two rather sharply defined groups. The larger,

TABLE 1.—*Analysis of Cases in Which Operations Were Performed*

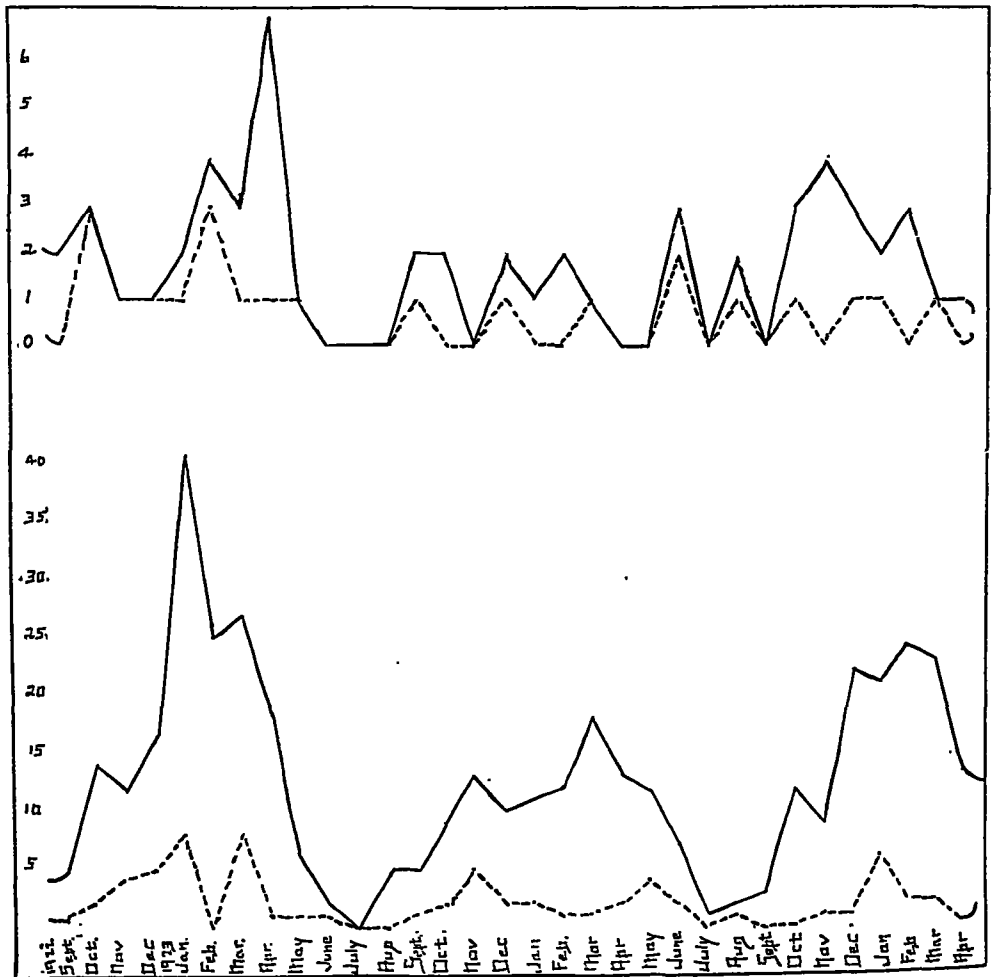
| | Number of Cases | Percentage |
|---------------------------|-----------------|------------|
| Bronchopneumonia..... | 22 | 31.9 |
| Lobar pneumonia..... | 20 | 28.9 |
| Acute bronchitis..... | 12 | 17.4 |
| Hypostatic pneumonia..... | 2 | 2.9 |
| Embolism..... | 11 | 16.0 |
| Massive collapse..... | 2 | 2.9 |
| Total..... | 69 | 100.0 |

consisting of fifty-six cases, presented lesions, lobar pneumonia, bronchopneumonia and bronchitis, in which infection certainly played a part. Fourteen of the fifty-six patients gave a history of an acute respiratory infection before operation, and in nine of these the operation was of an emergency character. This larger group showed a definite seasonal incidence, while the thirteen cases of the smaller group, including embolism and atelectasis, occurred scattered throughout the year with no suggestion of a seasonal variation.

In the accompanying chart the lower curves show the incidence of acute respiratory infection—pneumonia, tonsillitis, influenza and bronchitis—as observed in the medical division of the hospital during the period covered by this study. The solid line represents the total number of cases and the broken line the deaths. The upper curves illustrate the incident and the death rate in the surgical division of the group of postoperative, postanesthetic lobar pneumonia, bronchopneumonia and bronchitis. Because of the smaller number of cases in the surgical group the abscissa of the upper curves was made four times

greater than that of the lower in order to accentuate the variations. A rough parallelism between the two is readily seen.

It is probable that many of the patients admitted to a surgical service at a time when respiratory infections are prevalent in the community harbor the infectious organisms in their respiratory tracts. It is conceivable that any factor that lowers the patient's resistance, such as exposure or overfatigue, as well as the stress of operation and



Upper curves: postoperative respiratory complications in surgical division; lower: acute respiratory infections in medical division; solid line, cases; broken line, deaths.

anesthesia, might precipitate a pneumonia in such a person. Indeed, it has not been a rare occurrence to observe at such times the spontaneous development of pneumonia in patients who were being studied in the hospital preliminary to operation.

It would seem, therefore, that at a time when respiratory infection is epidemic in the community the surgeon should be conservative in recommending an operation of a nonemergency character, a precaution

that the nose and throat surgeon has long appreciated and observed. The patient should be observed in the hospital for several days before operation rather than be brought to operation immediately after admission. The presence of even a slight cold should be considered at such times a contraindication to anesthesia.

At such times, also, unusual precautions should be taken in the sterilization of the anesthetist's armamentarium, in the restriction of visitors, and in preventing physicians, nurses and attendants suffering with colds from coming in contact with the surgical patient. It is only necessary to refer to the 30 per cent mortality in the infectious group of respiratory complications to show the importance of these precautions.

The temperature records of the patients in this series were studied for possible information as to the factor of chilling. Eleven of the sixty-nine patients were returned from the operating room with a subnormal temperature, 97 F. or below, which persisted for from three to

TABLE 2.—*Incidence of Subnormal Temperature After Operation*

| | Complicated | Uncomplicated |
|---|-------------|---------------|
| Total number of cases..... | 69 | 120 |
| Cases with subnormal temperature after operation..... | 11 | 6 |
| Percentage..... | 16 | 5 |

TABLE 3.—*Sex and Ward Incidence*

| Ward | Cases | Deaths |
|-------------------|-------|--------|
| Men's ward 1..... | 28 | 9 |
| Men's ward 2..... | 1 | 0 |
| Women's ward..... | 9 | 3 |

fifteen hours. These patients were not in a state of surgical shock so that this factor as a cause of subnormal temperature may be eliminated.

For comparison, the records of 120 operative cases having no respiratory complications were taken at random, ten cases from each month over the period of a year. Only six of these showed a subnormal temperature and it lasted six hours or less.

The surgical division has two men's wards and one women's ward. Men's Ward 1 and the women's ward have the same number of beds and are exactly alike in construction, having the same northern and eastern exposure, the one being situated immediately above the other in a new wing of the hospital. The number of patients treated per year in the women's ward is distinctly greater than that in the men's ward, yet the incidence of respiratory complications is three times greater among the men than among the women.

This striking difference in sex incidence is noteworthy. Various factors may play a part in its production. It is possible that women

have a higher natural immunity to respiratory infection (which someone has recently attributed to the "hardening" that women undergo as a result of modern dress). Because of their more sheltered existence it is also possible that they are less exposed to epidemic infections, and therefore are less likely to harbor the infectious organisms at the time of admission to the hospital. We have found no confirmation of the sex incidence in the literature.

Men's Ward 2 is situated in an older section of the hospital with a southern exposure and is flanked on the east and west by two wings that prevent the direct access of high winds. Its bed capacity is greater than that of either men's Ward 1 or the women's ward, but the number of patients in it per year is smaller. However, the type of patient in this ward presents a poorer surgical risk than those in the other wards, including, as it does, all septic cases. The small incidence in this more protected ward is therefore striking. It is worth considering in the planning of hospital construction that in our striving for light and ventilation we may be unwittingly adding harmful exposure.

TABLE 4.—*Mortality*

| | Number of Cases | Deaths | Percentage |
|---------------------------------------|-----------------|--------|------------|
| I. Infectious group (pneumonia, etc.) | 56 | 22 | 39.9 |
| II. Embolism; collapse..... | 13 | 6 | 46.1 |
| Total..... | 69 | 28 | 40.6 |

MORTALITY

The gravity of postanesthetic, postoperative pulmonary complications is obvious from the foregoing figures. We have attempted to determine some of the factors that play a part in this high death rate.

TABLE 5.—*Length of Anesthesia and Mortality*

| Anesthesia | Recovered | Died | Per Cent |
|------------------------|-----------|------|----------|
| 15 to 30 minutes..... | 14 | 2 | 14.3 |
| 31 to 90 minutes..... | 28 | 13 | 46.4 |
| 91 to 240 minutes..... | 7 | 5 | 71.4 |

The danger of prolonged anesthesia, well known as it is, needs nevertheless to be constantly emphasized. Our figures show a distinct increase in the mortality of the complicated cases in direct proportion to the duration of the anesthesia.

TABLE 6.—*Age-Mortality Incidence*

| Age | Cases | Deaths | Per Cent |
|--------------------|-------|--------|----------|
| From 1 to 20..... | 7 | 2 | 28.5 |
| From 21 to 40..... | 30 | 12 | 40.0 |
| From 41 to 60..... | 23 | 8 | 34.7 |
| 61 plus..... | 9 | 6 | 66.7 |

There is little variation in the death rate in patients under the age of sixty. In the older patients, as might have been expected, the mortality is high.

TABLE 7.—*Anesthetics Used and Mortality*

| Anesthetic | Cases | Deaths |
|----------------|-------|--------|
| Local..... | 8 | 5 |
| Gas—local..... | 3 | 2 |
| Gas..... | 7 | 3 |
| Gas—ether..... | 13 | 2 |
| Ether..... | 24 | 10 |
| Spinal..... | 1 | 0 |

Our series is entirely too small to draw any conclusions as to the relative dangers of the types of anesthetic agent. However, in the infectious group of the complicated cases, gas-ether anesthesia carried a mortality well below the others, while local anesthesia had a surprisingly high death rate.

SUMMARY

The importance of the prevalence of acute respiratory infection in the community as an etiologic factor in postanesthetic, postoperative complications is emphasized. Attention is called also to the greater incidence of such conditions in men and to the possible part played by hospital ward construction and by chilling of the patient during operation. Prolonged anesthesia and advanced age both definitely increase the mortality.

A REVIEW OF UROLOGIC SURGERY

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Progress in Urology.—Braasch¹ reviews the recent progress in urology. He states that most of the present methods of treatment of submucous or Hunner's ulcers of the bladder are unsatisfactory. Surgical excision is frequently followed by recurrence. Various forms of lavage and topical applications also prove to be disappointing. Cauterization and fulguration frequently afford relief but not necessarily permanent cure. Braasch feels that alteration of the reaction of the urine deserves further study. He also considers the present views on the treatment of ureteral calculus and the indications for operation or cystoscopic manipulation and concludes by saying: "When a surgeon is available who has the ability to carry out either procedure, ureterolithotomy, which is attended by little or no mortality, and usually delays the patient but two or three weeks, is often to be preferred to the frequently tedious attempts at manipulative methods." Radium, in Braasch's estimation, has not proved as satisfactory in the treatment of carcinoma of the prostate and tumors of the bladder as it once was thought to be. A proper gradation of the malignancy of a vesical tumor and close observation of the patient following treatment will do much to standardize our methods of treatment.

In considering ureteral stricture, he does not look with favor on the indiscriminate dilatation of the ureter in all cases of vague abdominal pain, but in cases in which a stricture can be definitely shown by the urogram, he considers it to be a proper procedure.

Mercurochrome for intravenous use is found most beneficial in the more acute infections of the urinary tract and less so in chronic and gonorrheal infections. He considers the use of hexylresorcinol as still in the experimental stage.

1. Braasch, W. F.: A Review of Recent Progress in Urology, *J. Urol.* 14: 183-192 (Aug.) 1925.

KIDNEY

Surgical Technic.—Rosenstein,² after reviewing in a critical manner the advantages and disadvantages of the various extraperitoneal approaches to the kidney, advocates an incision that begins 8 cm. laterally from the spinous process of the first lumbar vertebra and extends to a point 14 cm. back from the anterior superior spine of the ilium. Cutting through the underlying latissimus dorsi and superficial lumbodorsal fascia brings the operator to the lumbar triangle (*Spatium tendineum lumbale*) bounded anteriorly by the muscles of the abdominal wall and posteriorly and above by the iliocostal and serratus posticus inferior. The floor of this triangle containing the deep lumbar fascia is incised, exposing the fatty capsule of the kidney. The incision is extended up to the last rib. The last intercostal arteries and nerves and the ilio-inguinal and iliohypogastric nerves are drawn aside, the latter toward the iliocostal muscle. By incision of the fatty capsule of the kidney the latter is easily exposed. In cases in which there is too small a space between the last rib and the iliac crest, resection of the last rib to give better exposure is recommended.

[ED. NOTE.—The incision, which is based on a muscle-splitting principle, would seem to be a good one. It is a question, however, whether its advantages are really greater than that of the Mayo or posterolateral incision so widely coming into use in this country. The division of the lumbar muscles for exposure of the kidney is followed by prompt healing, and hernia through such incision is a rare occurrence.]

Alcock³ says that any procedure in extreme cases is justified if it improves the patient's condition more than it increases the difficulties of nephrectomy. The division of nephrectomy into two stages is indicated in only a small proportion of cases. When carried out, it is a procedure not infrequently forced on the surgeon after he has tried to perform primary nephrectomy. There are two definite surgical procedures advocated in two-stage nephrectomy: one is ligation of the renal pedicle transabdominally; the second is preliminary nephrostomy for drainage. The latter is at times necessary on account of difficulties which may arise during the course of an attempted primary nephrectomy. Chute divides the cases of secondary nephrectomy into two groups: the first is made up of those cases in which the operation was intentional, and in his series of twenty, nine fell into this group; the second comprises those cases in which the operation was forced on the operator, either by difficulties arising at the time of operation, or by

2. Rosenstein, Paul: Ein funktioneller Lumbalschnitt zur Freilegung der Niere, *Ztschr. f. urol. Chir.* 17:119-126, 1925.

3. Alcock, N. G.: A Few Cases of Two-Step Nephrectomies. *J. Urol.* 14: 239-248 (Sept.) 1925.

errors of some sort either in diagnosis or judgment. He feels that two-stage nephrectomy in a very limited group of cases of renal infection is life saving. He brings out many valuable points in the technic, such as the inclusion of the sinus in the second incision, the necessity of freeing the kidney posteriorly first, the care to be taken in the reflection of the peritoneum, and the difficulties met with in dealing with the renal pedicle. In dealing with the pedicle he prefers, if possible, to ligate the entire pedicle before a clamp is put on, and then to follow this with the reinforced ligatures. He says that the preliminary nephrostomy makes the secondary nephrectomy more difficult, and that the difficulty is increased by the time that elapses between the first and the second operation. Alcock has performed preliminary nephrostomy in fifteen cases, and secondary nephrectomy in two. In one case, preliminary drainage had been carried out by another surgeon. In one series of ten cases, in which two-stage nephrectomy was premeditated, there were four cases of renal tuberculosis, two cases of pyonephrosis and four cases of hydronephrosis associated with infection. All these patients were in bad condition and preliminary drainage by catheter had been attempted. Two of the patients with tuberculosis never reached the second operation. In four of the remaining eight cases the kidney was removed. The other four patients are now in the interval between the two operations. Improvement of the general condition after the preliminary operation usually is very marked.

The removal of the kidney usually is not difficult and there is no greater loss of blood than would occur with primary nephrectomy. In five cases Alcock started with the intention of performing primary nephrectomy and either met with difficulty during the first operation or the patient's general condition became so serious that continuation of the operation was undesirable. Drainage of the kidney was effected in these cases. In two cases of renal tuberculosis in which nephrostomy was performed the general health of the patient was so much improved that consent to the second operation was refused. Alcock believes from the study of these cases that nephrostomy, as a preliminary step to nephrectomy in cases of infection of the kidney, is clearly indicated in a small group of cases. Preliminary nephrostomy makes the freeing of the kidney more difficult, but the decrease in the size of the kidney, the improvement in the patient's general condition and the decrease in the tendency to hemorrhage compensate for the increased difficulty. The sinus, if possible, should be included in the second incision. The kidney should be freed posteriorly first, and then around the lower pole, and the greatest care is necessary in reflecting the peritoneum. It is safest, if possible, to ligate the pedicle with one ligature before clamps are put on. After that, any further procedures possible in controlling the hemorrhage from the pedicle are to be recommended.

healthy kidney first. If no lesions are visible, urine should be collected by puncturing the renal pelvis, thus ruling out the possibility of infection. If the diseased kidney is exposed first the wound should be momentarily packed and the other side explored. This operation may be performed in either one or two stages, depending on the patient's condition. In exploration of kidneys in which the condition was unknown Cifuentes performed ureterotomy in seven cases. In four the exploration was unilateral: in two of these nephrectomy was performed, followed by death in one case. In three cases bilateral exploration was carried out; bilateral lesions were present in all and death occurred in all. Bilateral exploration of the kidneys was carried out in eighteen cases, in fifteen of which nephrectomy was performed; death occurred in one case, and cures followed in fourteen.

Nephrolithiasis.—Jean⁶ reports the case of a young man who had suffered from pain in the right side of the abdomen, hematuria and frequency for three years. Appendectomy had not changed his condition. Roentgenograms revealed a large shadow which was interpreted as an enlarged kidney. Ureteral catheters were passed up to a point 24 cm. above the orifices on both sides; 80 cc. of urine was obtained from the right renal pelvis, the last drops being thick pus containing staphylococci; the urine from the left side was normal. A diagnosis of right uronephrosis with infection was made. At operation it was impossible to locate the kidney through the usual lumbar incision. The incision was then prolonged to the right iliac fossa where an enlarged kidney was found, firmly adherent to the surrounding organs. Its anterior surface was lying against the posterior surface of the bladder; its external border was in contact with the right common iliac vein; its internal border was adherent to the rectum. No suprarenal body was found. The kidney was removed and the patient recovered uneventfully. Pathologic examination showed a pyonephrotic kidney with a stone 1 cm. in diameter in one of the calices near the hilum. This variety of anomaly is rare; only about fifty cases have been reported. Jean says that hydronephrosis is quite common in ectopic kidneys; the proximity to infected organs is probably the cause of the infection; lithiasis occasionally occurs; errors of diagnosis are numerous. He believes that the diagnosis should have been made in his case on account of the presence of an atrophic testis, but he was misled by the roentgenogram and by the fact that the ureteral sound had been passed up to at least 24 cm., whereas the ureter was only 6 cm. in length on the affected side. He deduces from this experience that a roentgenogram of the whole urinary tract and a pyelogram should be taken in all such suspected cases.

6. Jean, G.: Uropyonéphrose et lithiase d'un rein en ectopic iléo-pelviennne. J. d'urol. méd. et chir. 19:136-139, 1925.

plantar reflexes were lost, and the tendon of Achilles tenderness was lost. The vibratory sense was present in the ankles. The pain sense was lost below the level of the umbilicus on the right and to about 2 inches (5 cm.) above the umbilicus on the left. A neurologic examination by Dr. John L. Garvey, September 7, revealed that the patient complained of no pain in the lower extremities but now had a sensation of needles touching but causing no pain in the legs. He also complained, as before operation, of burning and jerking of the legs. The right patellar reflex was normal, the left diminished, and the Achilles tendon reflex was diminished. The plantar reflex was normal on both sides. The vibratory sense was present. The tendon of Achilles tenderness was lost. The sense of motion and position was normal. The pain sensation was lost to the umbilicus on the right, to just below the umbilicus on the left (fig. 24). There was no motor paralysis but the patient would not try to walk, going about in a wheel chair. Shortly thereafter he was persuaded to walk.

The patient returned to the hospital, Jan. 21, 1926. He had had no return of the former pain in the legs but had had sharp, intermittent pains in the chest, the abdomen, the shoulders and the upper part of the arms. He still had burning in the legs, most severe on the left. On the right, only the posterior aspect from the middle of the thigh down was involved. He had jerking of the feet and toes when recumbent but not when sitting or standing, and had incontinence of urine. He now used crutches because the "knees gave way." On neurologic examination, Jan. 25, 1926, the umbilical reflexes were not obtained. The patellar reflexes were active and equal; the tendon of Achilles reflexes were present, more prompt on the right. Plantar irritation caused extension of the toes on the right, no movement on the left. The tendon of Achilles tenderness was lost on both sides. The vibratory, motion and position senses were normal. The tactile sense was normal. The pain sense was lost to the level of the umbilicus on the right and to an ascending line 2 inches (5 cm.) above the umbilicus on the left. The temperature sense was lost below a horizontal level just beneath the umbilicus (fig. 26).

A positive diagnosis was not made. The patient, however, was greatly relieved by the loss of the excruciating pain which radiated from the inguinal region down both legs. The presence of a burning sensation in an area in which both pain and temperature sensations are completely lost is difficult to explain. A point of interest was the difference in the levels of analgesia and thermanesthesia, the former being a segment higher on the left and a trifle higher on the right. The reverse has been noted in a previous chordotomy case.

RÉSUMÉ

The series of nineteen cases that appear in the American literature embrace the reports of Martin and Spiller, Beer, Frazier, Leighton, and Frazier and Spiller. The operation has also been performed by Elsberg, Ernest Sachs and others in this country but the cases have not been published. The primary conditions in the foregoing series which ultimately made operation for the relief of pain necessary were: primary malignant disease of the spine, three; gunshot injury of the spine, three; tabes dorsalis, three; myelitis, two; carcinoma of the rectum, two; carcinoma of the cecum, one; carcinoma of the uterus, one; carcinoma of the breast, one; sarcoma of the thigh, one; shell wound of the sciatic

nerve in the pelvis, one; pain in the vagina and rectum, unknown origin, one. Most of the malignancies have metastasized to the spine or to the pelvic glands with direct involvement of the lumbosacral plexus.

There was satisfactory relief in fourteen, partial relief in five cases. By satisfactory relief was not necessarily meant complete absence of pain, judging from the records. Actual complete absence of pain was, however, obtained in most of those listed as satisfactory. One patient required three operations before even approximately satisfactory relief was obtained. Unilateral chordotomy was performed in six cases, bilateral in twelve. One of the latter had the two anterolateral columns sectioned at different times.

Little data relative to the area of analgesia which should be expected following section of an anterolateral tract can be obtained from some of the reported cases. This is partially due to the indiscriminate use of the cord segments as synonymous with the vertebrae. For example, the operation is reported as a section at the level of the sixth dorsal segment when as a matter of fact it was the sixth dorsal spinous process or perhaps the fifth dorsal which had been removed, placing the actual division of the cord at the eighth or ninth dorsal segment. We realize that a definite variation does exist between a given vertebra and the numerically corresponding segment. For this reason, we have mentioned in the abstracts of the foregoing cases the number of the spinous process removed during the laminectomy whenever such data was reported.

Section of the anterolateral tracts to control pain was, until recently, little used by European surgeons. The early reports embrace only four cases. Nonne operated in three cases of tabes; one patient received relief; one developed a paraplegia, and one died from the operation. Tietze at Förster's request operated successfully in one case. Recently, Sicard and Robineau¹³ reported twelve patients operated on in the previous year. The results were on the whole satisfactory.

Our series of nineteen cases embrace the following primary conditions: carcinoma of the uterus or cervix, nine; carcinoma of the breast, two; sarcoma of the leg, two; carcinoma of the prostate, one; carcinoma of the lung, one; retroperitoneal malignancy, one; pain in the legs associated with spasmodic contractions, one; pain in the legs of unknown origin, one, and avulsion of the lumbosacral plexus (traumatic sciatic neuralgia), one. The cases of carcinoma of the uterus or cervix had extensive pelvic metastases, probably with direct involvement of the lumbosacral plexus. The two cases of carcinoma of the breast, the two of sarcoma of the femur or tibia and the one of carcinoma of the lung had metastases to the vertebrae.

13. Sicard and Robineau: Cordotomie laterale anterieure pour Algies incurables, *Rev. neurol.* 1:21 (Jan.) 1925.

Two patients required a second chordotomy; one had relief for only ten days after the first operation; the other had no relief from the first chordotomy although the area of distribution of the great sciatic nerve was analgesic. Both had complete relief after the second operation. A third patient had three chordotomies, the first two giving analgesia only in the distribution of the sciatic nerves. One, case 19, actually had two chordotomies but was not listed as a failure at the first since the section of the anterolateral tracts was made in a lumbar segment, primarily to determine the resulting analgesia and was only incidental to an exploratory laminectomy.

The final results in our series of nineteen cases were: complete relief of original pain in sixteen; partial relief in two, and complete but apparently temporary relief in one. A bilateral chordotomy was performed on seventeen, a unilateral on two patients. Rhizotomy was combined with unilateral section of the anterolateral tracts in one case and with bilateral section in another.

Numerous interesting observations have been made in these nineteen cases. The level of analgesia must, of course, be below the segment of the cord sectioned, but beyond this self-evident fact the loss of pain sense may bear no relation to the segment incised. Rather it is the depth of the incision, particularly in the anterior portion of the anterolateral tract, which determines how closely the level of analgesia approaches the level of sensory distribution of the segment operated on. Illustrative examples are cases 1, 6, 9, 12 and 17. In case 1 bilateral section at the eighth dorsal segment resulted in loss of pain and temperature below the eleventh dorsal segment on the left side and only diminished pain on the right. The incision was made 2.5 mm. deep on the right while the left tract, which carries the fibers from the right leg, was divided slightly less deeply. In case 6, a bilateral chordotomy between the sixth and the seventh dorsal segments resulted only in loss of pain and temperature sensation in the distribution of the great sciatic nerve. A second chordotomy at a slightly greater depth gave much higher analgesia. Case 12 presents the most striking example: two bilateral chordotomies at a depth of 3 mm., the first at the sixth and the second at the third dorsal segment, resulted only in analgesia of the region of the distribution of the sciatic nerve in the lower part of the legs (figs. 10 and 11). However, a third chordotomy 0.5 mm. deeper, although at a lower level, gave a much higher analgesia and therm-anesthesia.

The highest level of lost pain and temperature sensation was obtained when the incision of the cord extended directly forward through the anterior root as in case 18. This resulted in a level of analgesia and therm-anesthesia approximating closely the level of sensory distribution of the segment operated on.

The level of lost pain sensibility may or may not correspond to the level of lost temperature sense. As a rule, these two sensations are lost in approximately the same area. Pain perception may, however, be lost at a higher or lower level than temperature (figs. 9 and 15). Isolated areas of preserved pain or temperature sense may occur in regions otherwise completely anesthetic to these sensations. In some patients, we noted a disturbance of pain or temperature sensations, the perceptions being either greatly diminished, frequently but irregularly lost, or usually misinterpreted.

A peculiarity noted in some patients was the interesting observation that the original pain of which the patient complained was lost although the area to which it had been referred was not completely analgesic. We have also noted occasionally that a pin point may be distinguished from a pin head although the sense of pain from the pin prick is absent. The tickle sense may be pronounced on the sole of the foot even when this area is completely analgesic.

The cutaneous and deep reflexes are not changed by section of the anterolateral tracts. When any of these reflexes are modified it means that the incision was carried too far posteriorly or that the operative manipulations have directly injured the crossed pyramidal tracts. Motion of the extremity should not be affected and any loss must be attributed to the same factors that affect the reflexes. Tactile sensation has never been changed in any of our series. Likewise, the senses of motion and position, vibration and localization are preserved.

OPERATION

The operation offers no special difficulties to the neurologic surgeon but it is not advocated for the surgeon who is not experienced in the special technic of intraspinal surgery. The exact level at which chordotomy should be performed varies somewhat with the case. It is essential that the division of the anterolateral tracts shall be at least four segments above the area to be rendered analgesic. This is to assure crossing of all the afferent fibers. In cases of upper abdominal pain we have added to the chordotomy division of the posterior nerve roots in the exposed field. This adds about one segment to the area of analgesia and protects against the possibility of some fibers crossing at a higher level than was anticipated. As a general rule, we have made the anterolateral tract division at the level of the fourth, fifth or sixth dorsal vertebrae. The cord at this level is more easily accessible than at other levels and analgesia should be obtained below the eighth to the tenth dorsal segment. Usually three posterior spinous processes are removed together with the laminae, as adequate exposure is essential. Occasionally only two laminae need be removed, the exact number depending on the depth of the wound. The dura is incised practically the entire length of the bony opening. The arachnoid is then carefully

and freely opened so that the operative procedure can be done from within the arachnoid. This is essential as the presence of the arachnoid anterior to the dentate ligament, should it lie against the cord, makes exact attachment of the dentate ligament and of the emergence of the anterior root obscure. A dentate ligament attachment is then divided, the dentate ligament grasped with fine forceps and the cord carefully rotated, exposing its anterolateral aspect.

Two methods may be used in dividing the cord: Either the Frazier chordotomy needle or hook may be inserted and then incision made against the hook, using this special instrument as a guide to the needed depth, or a very fine pointed, sharp knife can be inserted directly. The knife should be marked so that a depth of 3 mm. can be definitely determined. In our earlier operations, we followed Frazier's technic and divided to a depth of only 2.5 mm. We have found that 3 mm. gives more satisfactory results. Incision is made just anterior to the dentate ligament reflection from the cord, carried almost directly medially, but slightly forward, to a depth of 3 mm., and brought out through the origin of a motor root. I think it essential that at the level of the emergence of an anterior root the incision should be at a depth of from 2 to 2.5 mm.; i. e., the point of the knife, starting at a depth of 3 mm. in front of the dentate ligament should be carried directly forward parallel to the anteroposterior axis of the cord so that the point of the knife will appear at the median side of the anterior root, the particular fibers coming off at this level being divided. Little, if any, bleeding results from the cord incision. When bilateral chordotomy is indicated, the dentate ligament on the opposite side is grasped after division of its attachment to the dura, the cord rotated and a similar procedure carried out. The dura is then closed with a continuous silk suture and the muscle planes with interrupted sutures.

Throughout the operation no pressure should be brought on the cord. All sponging should be with cotton pledgets and no traction made on either anterior or posterior roots beyond that necessary to assure proper rotation of the cord. The use of suction apparatus almost entirely eliminates the necessity of sponging and materially facilitates the performance of the more delicate parts of the operation. We have found it advisable in certain selected cases to divide the three posterior nerve roots exposed in the field. If a unilateral chordotomy is being performed, the posterior nerve roots of the opposite side would be the ones divided. The two technical points, however, which we wish to emphasize especially are the complete freeing of the cord from the arachnoid and the division of the anterior median portion of the anterolateral column.

The postoperative treatment has not differed from that following laminectomy. If difficulty in urination is encountered, I have thought it advisable to empty the bladder by pressure above the pubis rather

than by catheterization. With the short laminectomy necessitated by this operation, the patients can be turned from side to side without difficulty. Frequently the patients complain of some pain on moving the arms when the incision has been made over the third, fourth and fifth dorsal vertebrae. This pain is referred directly to the operative wound and generally disappears within a few days.

Following unilateral division of the anterolateral tracts properly performed, there should be complete loss of pain and temperature sense on the opposite side up to a level of from three to five segments below the level of section. At times, the area of analgesia is still higher. Particularly is this true if the incision extends, as I now believe it should, through the anterior root as in case 18, in which the level of analgesia and thermesthesia is practically the same as the level of cord section. On the other hand, the area may be much lower, probably because certain fibers had not yet crossed, or the incision had not been carried to a sufficient depth.

CONCLUSIONS

Section of the anterolateral tracts is a justifiable operation to relieve intractable pain. In cases of malignant disease it is comparable to the more common palliative operations such as gastro-enterostomy in carcinoma of the stomach.

Rhizotomy alone has not given satisfactory relief of pain. It may be combined with chordotomy to insure a high level of analgesia.

Section of an anterolateral tract should give analgesia and thermesthesia on the opposite side up to a level approximately from three to five segments below the tactile distribution of the segment incised. Extending the section through the base of an anterior root may give loss of pain and temperature sense to a level corresponding closely with the segment operated on.

The motor function should not be impaired. Tactile, vibratory, localization, deep pressure and motion and position perceptions are preserved. Cutaneous and tendon reflexes are unchanged.

The chordotomy should extend to a depth of 3 mm. immediately in front of the dentate ligament and pass directly forward through the exit of fibers of an anterior root. This carries the incision to the anterior horn and just to the median side of a motor root. Bilateral section of the anterolateral columns should be performed when pain is confined to one side if the nature of the lesion is such that bilateral pain will probably soon appear. .

In a series of nineteen cases of my own and nineteen cases in the literature, reviewed here, the majority of the results were satisfactory.

Chordotomy with section of the anterolateral columns is the preferable means at our disposal to relieve intractable pain in the lower half of the body.

WOUNDS OF THE HEART

THE TECHNIC OF SUTURE *

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I. INTRODUCTION

The successful suture of a wound of the heart is not an uncommon surgical feat. To the individual surgeon, however, the experience of performing the operation is rare, and the subject may therefore receive but little consideration until the occasion for carrying out the operation is presented. In the numerous case reports of suture of wounds of the heart little attention has been directed toward the method of placing the sutures for the closure of the wound. "The surgeon having this job in hand will take it all in the day's work, and just as he plunges his hand into the abdomen into a mass of blood in a case of ruptured spleen or in a case of ruptured tubal gestation and seizes the bleeding spot, so he will now plunge his hand into the pericardium and seize the heart, and, by digital compression, control the hemorrhage, and proceed to suture the wound."¹

The purpose of this article is to review certain phases of the subject and to present a method that may aid in the suture of wounds of the heart.

II. HISTORY

The history of wounds of the heart may be divided into the following periods:

1. The period of mysticism in which wounds of the heart were considered necessarily fatal. It extended into the seventeenth century.
2. The period of observation and experiment.
3. The period of suture, beginning in 1882.

1. PERIOD OF MYSTICISM

The Heart is the chiefe mansion of the Soule, the organe of the vitall faculty, the beginning of life, the fountaine of the vitall spirits, and so consequently the continuall nourisher of the vitall heate, the first living and last dying, which because it must have a naturall motion of itself, was made of dense solide and more compact substance than any other part of the body.²

* From the Laboratory of Experimental Surgery, the Western Reserve School of Medicine and the Lakeside Hospital.

1. Ballance, C. A.: The Bradshaw Lecture on the Surgery of the Heart, delivered before the Royal College of Surgeons, Dec. 11, 1919, London, Macmillan Company, 1920.

2. Paré, Ambrose: The Workes of That Famous Chirurgion Ambrose Parey, translated by T. Johnson, London, T. Cotes, 1634.

The story opens with the legends of Homer³ about the ninth century B. C. In the Iliad is recorded the observation of the movements of the heart transmitted through a spear that had transfixed the heart of Alkathoos. "The hero Idomeneus smote him in the midst of the breast with the spear. . . . And he fell with a crash, and the lance fixed in his heart, that, still beating, shook the butt end of the spear." Again, Homer,⁴ in his narration of the death of Sarpedon, sang:

Not so Patroclus' never erring dart;
Aim'd at his breast, it pierced the mortal part,
Where the strong fibers bind the solid heart.
Th' insulting victor with disdain bestrode
The prostrate prince, and on his bosom trod;
Then drew the weapon from his panting heart,⁵
The reeking fibers clinging to the dart;
From the wide wound gush'd out a stream of blood,
And the soul issued in the purple flood.

Hippocrates⁶ stated that "a severe wound of the bladder, of the brain, of the heart, of the diaphragm, of the small intestine, of the stomach and of the liver is deadly," but he did not emphasize any special danger of wounds of the heart as did later writers. Wounds of the heart undoubtedly occurred in the great Persian wars and in the subsequent struggles for supremacy in Greece. Aristotle, Ovid, Celsus Pliny and Galen regarded them as *absolutely and necessarily fatal*.

Aristotle⁷ said:

The heart alone of all the viscera cannot withstand serious injury. This is to be expected because when the main source of strength (the heart) is destroyed there is no aid that can be brought to the other organs which depend upon it.

3. Homer: The Iliad, xiii, line 442, translated by Lang, Leaf and Myers, New York, Macmillan Company, 1922, p. 259.

4. Homer: The Iliad, xvi, lines 588-625, translated by Alexander Pope, London, George Bell & Sons, 1904, p. 299.

5. In 1898 Empress Elizabeth of Austria perished suddenly on the withdrawal of a file from the heart. Death was due to compression of the heart by the collection of blood in the pericardial cavity. Had the signs of increased intrapericardial pressure been heeded, the wound undoubtedly could have been sutured. The procedure could have been carried out most safely if the heart had been exposed at operation before the file was withdrawn. But at this late date, recent as it may seem, the pulsating heart of the human being had been exposed to view only a few times and the veil of mystery (to the surgeon) was just being lifted.

6. Hippocrates: The Genuine Works of Hippocrates, Section 6, Aphorism 18, translated by Francis Adams, New York, William Wood & Co., 2:252.

7. Aristotle (384-322 B. C.): De partibus Animalium, Lib. III, cap. 4, Opera edidit Academia Regia Borussica 3:328.

Ovid ⁸ wrote:

Although Aesculapius himself applies the sacred herbs by no means can he cure a wound of the heart.

Celsus ⁹ stated:

When the heart is wounded much blood is lost, the pulse weakens, pallor becomes extreme, a cold and foul sweat arises from the stricken body, the extremities become cold and speedy death follows.

Pliny ¹⁰ said:

This is the only one among the viscera that is not affected by maladies, nor is it subject to the ordinary penalties of human life; but when injured, it produces instant death.

Wounds of the heart were observed in gladiators, and they were considered uniformly fatal, according to Galen: ¹¹

Inflammato autem manifeste corde; gladiatores vidimus haud aliter, quam qui cardiaca syncope pereunt, obiise. Igitur si ad ventrem cordis vulnus aliquando peneraverit, protinus magno cum sanguinis fluore moriuntur, idque praecipue, si sinistrae partis venter fuerit vulneratus; si vero non ad ventrem usque pertingat, sed in cordis substantia consistat vulnus, ex ita affectis aliqui non solum ea die, qua vulnerati fuerunt, sed sequenti quoque nocte vivere potuerunt, inflammationis ratione nimirum extincti; atque ii omnes quamdiu vixerint, mentis compotes sunt; unde evidens quoque sibi testimonium sumere potest antiqua secta, quae negat rationalem animae facultatem in corde consistere.

In the opinion of Paulus Aegineta, ¹²

When the heart is wounded, the weapon appears at the left breast and feels not as if in a cavity but as fixed in another body, and sometimes there is a throbbing motion; there is a discharge of black blood if it can find vent, with coldness, sweats, and deliquium animi, and death follows in a short time.

Fallopious ¹³ asserted:

Wounds of the heart are always followed by sudden death. When wounded it cannot heal, being too firm, always in motion, and of an inflammatory heat.

8. Ovid (43 B. C.-17 A. D.): *Epistolae ex Ponto*, Lib. I, Epist. III, lines 21-22.

9. Celsus (1st century A. D.): *Medicinae Libri Octo*, Lib. V, cap. 26, L. Targae, Lugduni Batavorum, by S. and J. Luchtmans, 1791, p. 307.

10. Pliny, the Elder (23-79): *Historia Naturalis*, Lib. XI, cap. 37, translated by Bostock and Riley, London, H. G. Bohn, 3:65, 1855.

11. Galen (130-200?): *Medicorum Graecorum Opera*, volumen VIII, Lipsiae prostat in officina Libraria car. cuoblochii 1824, *De locis affectis*, edited by D. C. Kühn, T. VIII, Lib. v, cap. 2, p. 304.

12. Paulus Aegineta (625-690): *The seven books of Lib. VI*, sect. 88, translated by Francis Adams, London, Sydenham Society, 1846, 2:421.

13. Fallopious (1523-1562): *Opera omnia tractatus de vulneribus in genere*, cap. 10, Frankfurt, 1600, p. 163.

Wounds of the right ventricle may be differentiated from wounds of the left ventricle; from the former comes dark blood, from the latter, red blood.

Paré¹⁴ wrote:

By these signs you may know that the heart is wounded: If a great quantity of blood gush out, if a trembling possess all the members of the body; if the pulse be little and faint, if the colour become pale, if a cold sweate and frequent sowning assaile him, and the extreme parts become cold, then death's at hand. Yet when I was at Turin I saw a certaine Gentleman who fighting a Duell with another, received a wound under his left breast which pierced into the substance of his heart, yet for all that he stricke some blowes afterwards, and followed his flying Enemie, some two hundred paces until he fell downe dead upon the ground; having opened his body, I found a wound in the substance of the heart, so large as would containe one's finger; there was onely much blood poured forth upon the midriffe.

According to Fabricius:¹⁵

If the heart is wounded the affair is desperate, so also if the pericardium is wounded. It is, therefore, unnecessary to attempt any treatment.

Zacchias (1584-1659), according to Fischer,¹⁶ reported a case of needle wound of the heart in which death did not occur until the sixth day after the injury, "*hoc quidem mirabile auditu est*" because "the noblest organ of the body cannot survive a solution of its continuity and this is the general medical opinion."

Boerhaave¹⁷ said:

All wounds of the heart deep enough to penetrate into either of its ventricles are mortal.

2. PERIOD OF OBSERVATION AND EXPERIMENT

The idea that all wounds of the heart were necessarily fatal, established by the ancient authority of Aristotle and Galen, remained unchallenged until the seventeenth century when there began a period of independent observation and experiment. It was the period in which Riolan and Harvey made their contributions and, a century later, Morgagni and Larrey.

According to Fischer,¹⁶ who carefully reviewed the early literature of the subject, the first to advance the idea that wounds of the heart

14. Paré (1509-1590): *The Workes of That Famous Chirurgion Ambrose Parey*, translated from the Latin by T. Johnson, London, T. Cotes, 1634.

15. Fabricius ab Aquapendente (1537-1619): *Opera chirurgica*, Cap. 21, Patavii, 1666, p. 104.

16. Fischer, Georg: *Die Wunden des Herzens und des Herzbeutels*, Arch. f. klin. Chir. 9:571, 1868.

17. Boerhaave (1668-1738): *De Vulnere in Genere*, *Aphorismi de Cognoscendis et Curandis Morbis*, Aphorism 170, p. 43.

can heal and that such wounds are not necessarily fatal was Hollerius¹⁸ (1498-1562), and the first authentic description of a healed wound of the heart was by Idonis Wolf¹⁹ in 1642. It took over a century, however, for this new conception to receive recognition.

Sénac,²⁰ in 1749, stated that wounds of the heart are always serious; nevertheless, a nonpenetrating wound may heal and may not be fatal. An important advance in the knowledge of the subject was made by Morgagni²¹ in 1761 by pointing out the danger of compression of the heart due to hemorrhage into the pericardium. Larrey,²² who had had considerable experience in the treatment of wounds of the pericardium and heart and who had performed some experiments on the heart in dogs, stated that the view generally held by physicians concerning these wounds was too grave. In 1829 he reported a case that he treated by passing a catheter into a stab wound of the chest; he obtained three beakers of wine colored fluid, and after the passage of a sound obtained four more beakers of similar fluid. This, according to Larrey, was the first case of a wound of the pericardium in which the patient recovered.

The treatment of wounds of the heart during the first half of the nineteenth century consisted of absolute quiet, the application of leeches, venesection, and the passage of a catheter or a sound into the wound for the evacuation of fluid from the pericardial cavity. Dupuytren²³ advised venesection to be carried out almost to the point of exsanguination. Jobert²⁴ in 1839 stated:

The duration of life is in proportion to the quantity of blood lost and especially to that which is contained in the pericardium. I have seen death occur promptly in one of these patients, not because of the extent of the wound, but because the blood which had been shed, not being able to escape through the narrow opening in the pericardium, compresses the heart and opposes the accomplishment of its function. This effect is produced only by a compression taking place suddenly and it does not take place in the same manner when the compression is established

18. Hollerius, J.: *Communis aphorismi allegati*, quoted from Fischer (Footnote 16).

19. Wolf, Idonis, cited by Fischer (Footnote 16).

20. Senac, J. B.: *Traité de la Structure du Coeur, de son Action, et de ses Maladies*, Paris, Briasson, 1749, 2:366.

21. Morgagni, J. B.: *De Sedibus et Causis Morborum*, Lipsiae sumptibus Leopoldi Vossii, 1829.

22. Larrey, D. J.: *Clin. Chir.*, Paris, 2:284, 1829.

23. Dupuytren, Guillaume: Clinical Lecture on Surgery, delivered during sessions of 1834 at the Hotel Dieu, Paris, *Leçons Orales de Clinique Chirurgicale on Wounds of the Heart: Their Varieties, Causes, Symptoms, and Treatment*, *Lancet* 1:767, 1834-1835.

24. Jobert, J. A.: *Réflexions sur les plaies pénétrantes du coeur*, *Arch. gén. de méd.* 6:1, 1839.

little by little, as in hydropericardium, for example. If the blood continues to be poured out of the cavities of the heart in great abundance, death will occur promptly, but here again the feebleness of the patient and syncope sometimes stop the beating of the heart, and there is formed a clot which opposes the further escape of blood.

Numerous case reports appeared during the remainder of this period. Cases were compiled, the clinical signs and symptoms were analyzed, and the pathology was studied. Purple²⁵ in 1850 compiled forty-two cases, eleven of which were from American sources. In 1868 appeared a comprehensive monograph by Georg Fischer¹⁶ with a compilation of 452 cases, only 10 per cent of which resulted in recovery. That wounds of the heart might be treated by suture was suggested, but not carried out, by Roberts²⁶ in 1881.

3. PERIOD OF SUTURE

The first experiments to suture wounds of the heart were performed by Block²⁷ on rabbits in 1882. Wounds made experimentally were sutured, with recovery of the animal, and the feasibility of applying the procedure to the human heart was suggested. The subject, however, was met with opposition. Thus, Billroth²⁸ in 1883 stated that "the surgeon who should attempt to suture a wound of the heart would lose the respect of his colleagues"; Riedinger²⁹ in 1888 wrote, "the suggestion to suture a wound of the heart, although made in all seriousness, scarcely deserves notice"; and Stephen Paget³⁰ in 1896 stated that "surgery of the heart has probably reached the limits set by Nature to all surgery: no new method and no new discovery can overcome the natural difficulties that attend a wound of the heart. It is true that 'heart suture' has been vaguely proposed as a possible procedure, and has been done on animals, but I cannot find that it has ever been attempted in practice." Little support was given to the procedure until 1895 when Del Vecchio³¹ demonstrated to the Eleventh International

25. Purple, S. S.: *Statistical Observations on Wounds of the Heart, and on Their Relations to Forensic Medicine*, with a table of forty-two recorded cases, New York J. M. & Collateral Sc. **14**:411, 1855.

26. Roberts, J. B.: *The Surgery of the Pericardium*, Ann. Anat. & Surg. **4**: 247, 1881.

27. Block: *Verhandlungen der Deutschen Gesellschaft für Chirurgie*, Elften Congress, Berlin, 1882, Part 1, p. 108.

28. Billroth, Theodore, quoted from Jeger, Ernst: *Die Chirurgie der Blutgefäße und des Herzens*, Berlin, A. Hirschwald, 1913, p. 295.

29. Riedinger: *Verletzungen und Chirurgische Krankheiten des Thorax und seines Inhaltes*, Stuttgart, Ferdinand Enke, 1888, Part 42, p. 189.

30. Paget, Stephen: *The Surgery of the Chest*, London, John Wright & Co., 1896, p. 121.

31. Del Vecchio, S.: *Sutura del Cuore*, Riforma med. **11**:38, 1895

Medical Congress at Rome healed wounds of the heart in dogs following suture. Almost within a year from this date three attempts to suture wounds of the human heart were made. The first was by Cappelen³² of Christiania, Sept. 4, 1895; the second³³ was by Farina³⁴ of Rome, March, 1896, and the third was by Rehn³⁵ of Frankfurt, Sept. 9, 1896.

CAPPELEN'S CASE

A man, aged 24, received a stab wound in the fourth left interspace in the midaxillary line. He walked home bleeding from the wound. About one hour later he was admitted to the hospital, at which time he showed signs of hemorrhage, an imperceptible pulse and distant, faint heart sounds. Bleeding from the wound had ceased. Camphor stimulated the heart so that the pulse could be felt and consciousness returned. There was dulness to percussion over the left side of the chest.

At operation chloroform anesthesia was used. The third and fourth ribs on the left side were resected. The intercostal artery was not cut. The left pleural cavity contained 1,400 cc. of blood. The lung was not injured. Bleeding continued from the depth of the operative field and an opening in the pericardium large enough to admit the tip of the finger was found. The pericardium was distended with blood. It was opened. A wound in the left ventricle 2 cm. long was sutured with chromic catgut and a bleeding coronary artery was ligated. The rhythm of the heart was regular throughout the operation.

During the postoperative period, which lasted two and one-half days, the pulse was rapid; cyanosis was present, and there was a slight fever. The cause of death was anemia and pericarditis. The wound had not penetrated into the cavity of the left ventricle. The bleeding had occurred from the coronary artery.

FARINA'S CASE

The first case of surgical interference on the heart which I had the opportunity of performing was carried out in March, 1896, at the Spedala della Consolazione. The patient was a man 30 years of age who received a blow from a very fine and sharp dagger in the fifth intercostal space in the parasternal line. The wound penetrated to the cavity in an oblique direction from above downwards and from without inwards. It wounded the pericardium and penetrated into the ventricle. The wound in the myocardium was about 7 mm. long. I removed the fifth costal cartilage and a bit of the rib for about 15 cm. Then I strongly retracted the fourth and sixth costal cartilages. I arrived on the wounded heart. I sutured the wound with three silk sutures, and between these particular points I placed two others of less importance. Everything went well till the fifth day, when a violent bronchopneumonia declared itself on the right side and in three days killed the patient. The thoracic wound healed by primary intention.

32. Cappelen, A.: *Vulnia Cordis, Sutur af Hjertet*, Norsk. Mag. f. Lægevidensk. **11**:285, 1896.

33. Most writers have given to Farina the credit for first suturing a wound of the human heart.

34. Farina: Discussion, *Centralbl. f. Chir.* **23**:1224, 1896.

35. Rehn, L.: *Ueber Penetrierende Herzwunden und Herznaht*, Arch. f. klin. Chir. **55**:315, 1897.

At the necropsy the wound in the heart was found perfectly healed. The heart was not allowed to be preserved for further study. It was precisely because of my irritation at this fact that I have not published any communication on this interesting case. (From a personal letter by Farina to John Bland Sutton, May, 1910.)

REHN'S CASE

A man, aged 22, was stabbed with a knife in the fourth interspace, three fingerbreadths to the left of the sternal margin. After a period of unconsciousness, which lasted three hours, the patient revived sufficiently to take about 300 paces, when he fell to the ground. He was later found almost lifeless and was taken to a hospital. The first day following the injury the sensorium cleared, the pulse became stronger and dyspnea decreased. During the second day, signs of extreme circulatory failure with cyanosis and marked dyspnea developed and the operation was performed.

An incision 14 cm. long was made in the fourth left interspace and the fifth rib was divided in the mammary line. The pleura was opened. Blood distended the pericardium and oozed from the stab wound which entered it. The pericardium was opened widely and the blood within it was removed. A wound 1.5 cm. long was found in the right ventricle from which there was active bleeding. This was controlled by placing a finger over the wound, but difficulty was experienced in keeping the finger properly placed. There was less bleeding during diastole than during systole. The wound was closed with three silk sutures placed during several diastolic phases. The pulse immediately improved. After the blood was removed from the pleural and the pericardial cavities an iodoform gauze drain was placed in each.

The patient recovered and was able to return to work.

Experiments by Bode³⁷ and Salomoni³⁸ further demonstrated the healing of such wounds following suture; and Elsberg,³⁹ by resecting a third of the heart in dogs and in rabbits, with subsequent recovery, showed that the heart could tolerate extensive surgical procedures.

There has appeared in the literature a large number of cases in which wounds of the heart have been sutured. Ten years after he had performed the first successful suture, Rehn⁴⁰ compiled 124 cases, in 40 per cent of which the patients had recovered, and in 1920 Tuffier⁴¹ assembled 305 cases, in 50.4 per cent of which the patients had recovered. A surgical procedure was thereby introduced which has decreased the mortality of wounds of the heart about 40 per cent.

37. Bode, F.: *Versuche über Herzverletzungen*, Beitr. z. klin. Chir. **19**:167, 1897.

38. Salomoni: *Beitrag zur Chirurgie des Herzens*, abst. in *Centralbl. f. Chir.* **23**:1224, 1896.

39. Elsberg, C. A.: *J. Exper. Med.* **4**:479, 1899.

40. Rehn, L.: *Zur Chirurgie des Herzens und des Herzbeutels*, Arch. f. klin. Chir. **83**:723, 1907.

41. Tuffier, T.: *La Chirurgie du Coeur*, Cinquieme Congres de la Societe Internationale de Chirurgie, Paris, July 19-23, 1920, *Extrait. Brussels, Hayez*, 1920.

III. HEART TAMPONADE

Compression of the heart by the collection of blood in the pericardial cavity is the cardinal sign in the diagnosis of wounds of the heart. The physiology of heart tamponade has received little attention in our medical schools and the subject merits discussion.

That the heart may be compressed by the collection of blood in the pericardial cavity and the circulation thereby embarrassed was mentioned first by Morgagni²¹ in 1761 and later by Jobert²⁴ and by Franck.⁴² In 1884 Rose⁴³ coined the term "herz tamponade" and presented cases of wounds of the heart that were fatal, not from exsanguination nor from the extent of the injury itself but primarily from compression of the heart by a relatively small amount of blood locked in the pericardial cavity. Experiments by Cohnheim⁴⁴ showed that an increased pressure in the pericardial cavity was accompanied by a fall in the arterial pressure and a rise in the venous pressure, and that these phenomena were brought about by the obstruction to the filling of the heart produced by the increased intrapericardial pressure. When this reached the level of the venous pressure, the heart, as shown by Kuno,⁴⁵ ceased to function.

In experiments performed by me, an increase in the intrapericardial pressure of a column of water 10 cm. in height was followed immediately by a fall in the arterial pressure and a rise in the venous pressure, and when the intrapericardial pressure was continued the result was fatal. On release of the intrapericardial pressure the arterial and venous pressures returned to the normal levels (fig. 1), the former sometimes showing a compensatory rise⁴⁶ of from 10 to 20 mm. of mercury above the normal level. During the tamponade the pulse pressure decreased, the heart rate increased, and the dog became cyanosed. Roentgenograms showed little or no increase in the cardio-pericardial shadow during the tamponade (fig. 2). This was to be expected, however, because the sudden increasing of the intrapericardial pressure by a column of water 10 cm. in height added only from 40 to

42. Franck, Francois: Sur le Mode de Production des Troubles Circulatoires dans les Epanchements Abondants du Pericarde, *Compt. rend. Soc. de biol.* **1**:1242, 1877.

43. Rose, E.: Herztamponade (Ein Beitrag zur Herzchirurgie), *Deutsche Ztschr. f. Chir.* **20**:329, 1884.

44. Cohnheim, J.: *Lectures on General Pathology*, London, New Sydenham Society, **1**:21, 1889.

45. Kuno, Yas: The Mechanical Effect of Fluid in the Pericardium on the Function of the Heart, *J. Physiol.* **51**:221 (Sept.) 1917.

46. In experiments on dogs the compensatory rise above the normal pressure did not occur regularly after release of the increased intrapericardial pressure; it occurred also after section of the vagi, after removal of the stellate ganglions, and after denervation of the heart.

50 cc. to the pericardial fluid and, further, the heart under an increased pericardial pressure contained less blood and was actually smaller than under the normal condition.⁴⁷

The rapidity with which the intrapericardial pressure formed was an important factor in determining the degree of tamponade. In experiments on dogs the injection of 150 cc. of fluid into the pericardial

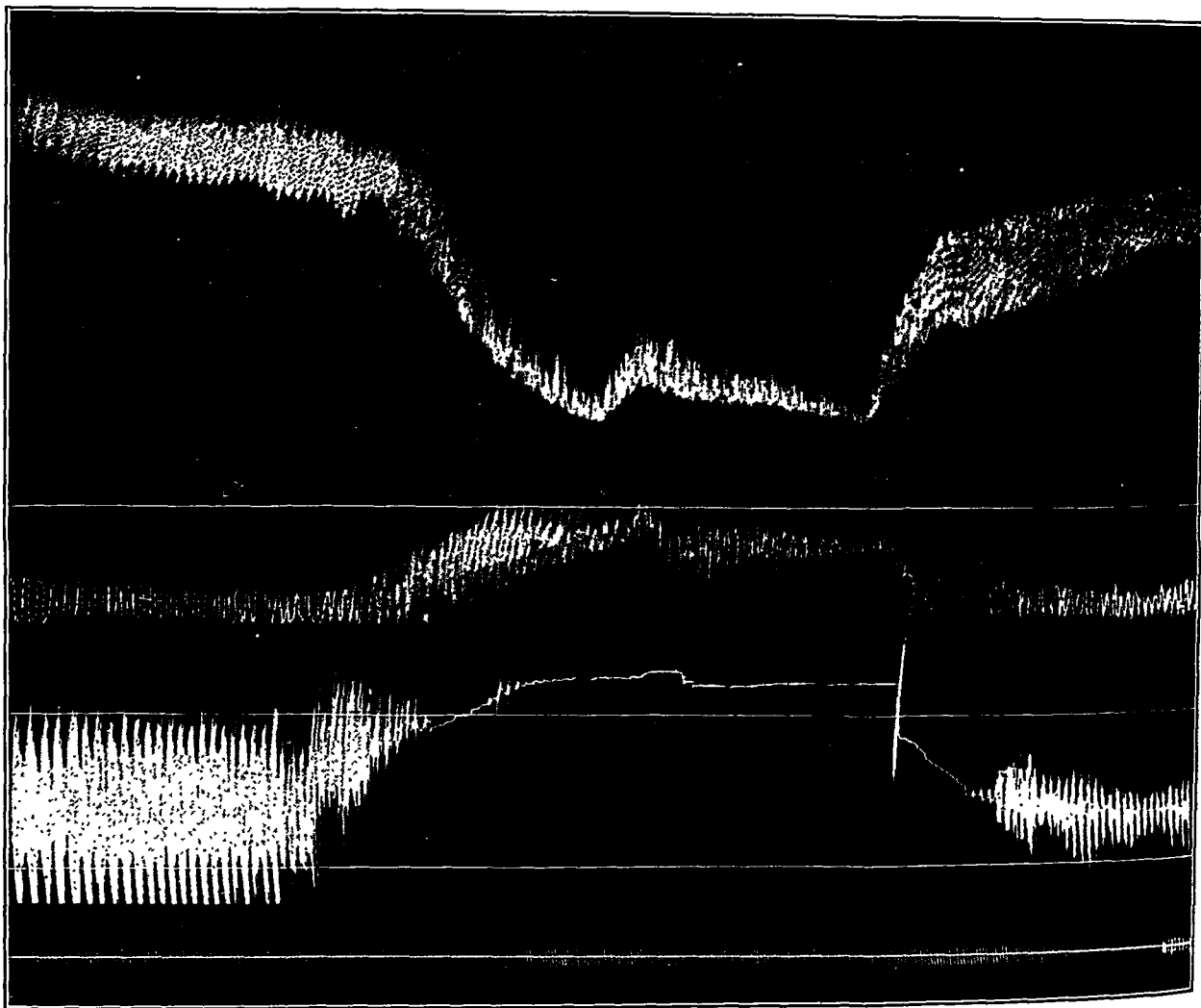


Fig. 1.—Effect of heart tamponade: upper curve shows arterial pressure, femoral; middle curve, venous pressure, innominate, and lower curve, intrapericardial pressure. The intrapericardial pressure was increased 10 cm. of water and caused a marked fall in the arterial pressure and a rise in the venous pressure; on release of the intrapericardial pressure the arterial and venous pressures returned to their former levels. The time is shown in seconds.

47. That the size of the heart decreased under increased pericardial pressure was observed in dogs that died from tamponade due to hemopericardium in experiments in which radium was used to produce mitral stenosis or metallic bands to produce aortic or pulmonic stenosis.

cavity over a period of thirty minutes was fatal. In stab wounds of the human heart in which the opening in the pericardium did not allow the escape of blood through it, 250 cc. produced a fatal tamponade. In cases of effusion in which the fluid formed gradually, from 2 to 4 liters were found in the pericardial cavity, as was reported in cases of scurvy in Russia.⁴⁸ In these cases the pericardium dilated and as its limit of elasticity was approached the intrapericardial pressure rose and when it equaled the pressure in the venae cavae, blood no longer entered the heart and the condition became fatal.

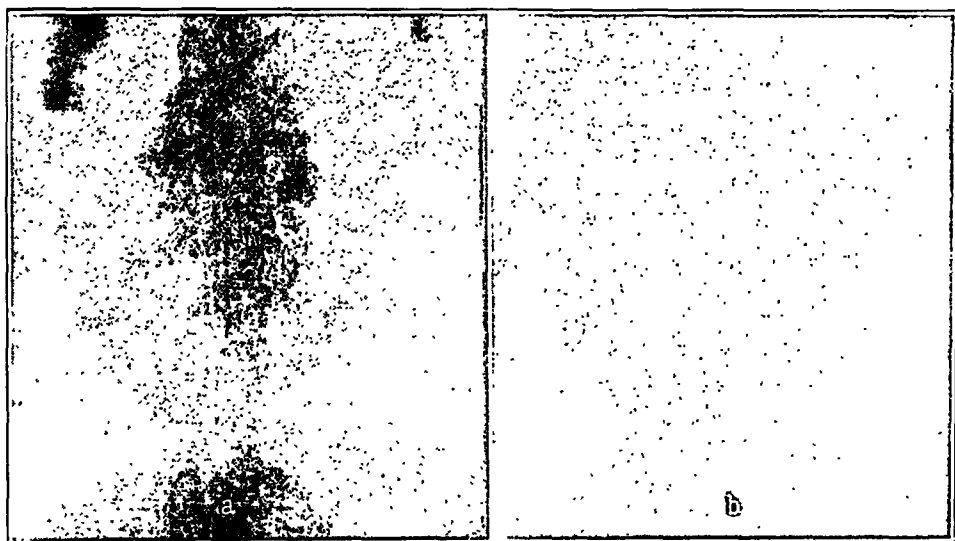


Fig. 2.—Heart of dog, weighing 12 Kg.; a cannula was tied into the pericardium and physiologic sodium chlorid solution was introduced; the roentgen-ray target and the film were at fixed distances from the heart; the position of the dog remained unchanged so that the cardiopericardial shadows permit accurate comparison; *a*, before increasing the intrapericardial pressure; *b*, after increasing the intrapericardial pressure by a column of physiologic sodium chlorid solution 10 cm. in height (sufficient to produce a fatal tamponade). The increase in the size of the cardiopericardial shadow is slight.

IV. OPERATIVE PROCEDURES

1. EXPOSURE OF THE HEART

Numerous methods for the exposure of the heart have been described in which incisions made in the midline parallel to the sternum were utilized, incisions made in various directions to the left or to the right of the sternum, and osteoplastic flaps in which one or more ribs were reflected. Of the various methods that have been proposed the most satisfactory are the median sternotomy and the left intercostochondral

48. Karanaeff, quoted from Kyber: *Paracentesis des Herzbeutels*, *Ztschr. Ruslands*, Saint Pétérshbourg, 21:161, 1847.

thoracotomy. The former provides the best exposure of the heart; the latter provides exposure of both the heart and the left lung.

*Median Sternotomy.*⁴⁹—The skin incision extends from the level of the second interspace to the midpoint between the umbilicus and the xiphoid. The xiphoid may be either removed or separated on one side from its ligaments and aponeuroses. The underlying structures are freed from the sternum, and a spatula is inserted beneath it to protect the heart. The sternum is split longitudinally with a saw or bone shear to the level of the second or third intercostal space, where it is cut across, care being taken to avoid the internal mammary vessels. The sternum is retracted, and the pleurae are dissected laterally with a moist sponge. The peritoneum is opened and the anterior portion of the diaphragm is incised. The pericardium is opened widely, the incision extending to its reflection on the diaphragm. An excellent exposure of the heart is obtained (fig. 3).

The structures are closed in layers. The sternum should be closely approximated with several silver wire sutures that encircle it.

The operation is not difficult to perform. It is well tolerated by the patient. It is the operation of choice in those cases of wounds of the heart that are not accompanied by a wound of the left lung, making exposure of the latter necessary. If the right lung is involved, exposure may be obtained through the midsternal incision by opening the right border of the mediastinum.

*Intercostochondral Thoracotomy.*⁵⁰—The incision is made in the left fourth intercostal space extending from the anterior axillary line to the sternum, where it is continued in each direction along the margin of the sternum to expose the third, fourth, fifth and sixth costal cartilages. These costal cartilages are sectioned; the internal mammary vessels are ligated, and the incision is extended through the underlying muscles into the pleura. The structures are retracted and the pericardium is opened. The left lung, the left ventricle, and part of the right ventricle are exposed (fig. 4).

Part of the right ventricle and the base of the heart, including the auricles, are not exposed. The transverse sinus and the venae cavae are inaccessible. The control of hemorrhage by compression of these struc-

49. Milton, H.: Mediastinal Surgery, *Lancet* 1:872, 1897. Rehn (Footnote 40). Duval, P., and Barasty, P.: De la Péricardotomie Thoracoabdominale médiane (Chirurgie du coeur et des gros vaisseaux de la Base), *Presse méd.* 26:437 (Aug. 29) 1918. Cutler, E. C.; Levine, S. A., and Beck, C. S.: The Surgical Treatment of Mitral Stenosis: Experimental and Clinical Studies, *Arch. Surg.* 9:689 (Nov.) 1924.

50. Spangaro, S.: Sulla tecnica da seguire negli interventi chirurgici per ferite del cuore e su di un nuovo processo di toracotomia, *Clin. chir.* 14:227, 1906.

tures, therefore, cannot be carried out when this exposure is used. The exposure is sufficient, however, to permit direct compression of the ventricles in the grasp of the operator.

To increase the exposure of the heart it has been suggested that the second costal cartilage be divided and that the sternum be split

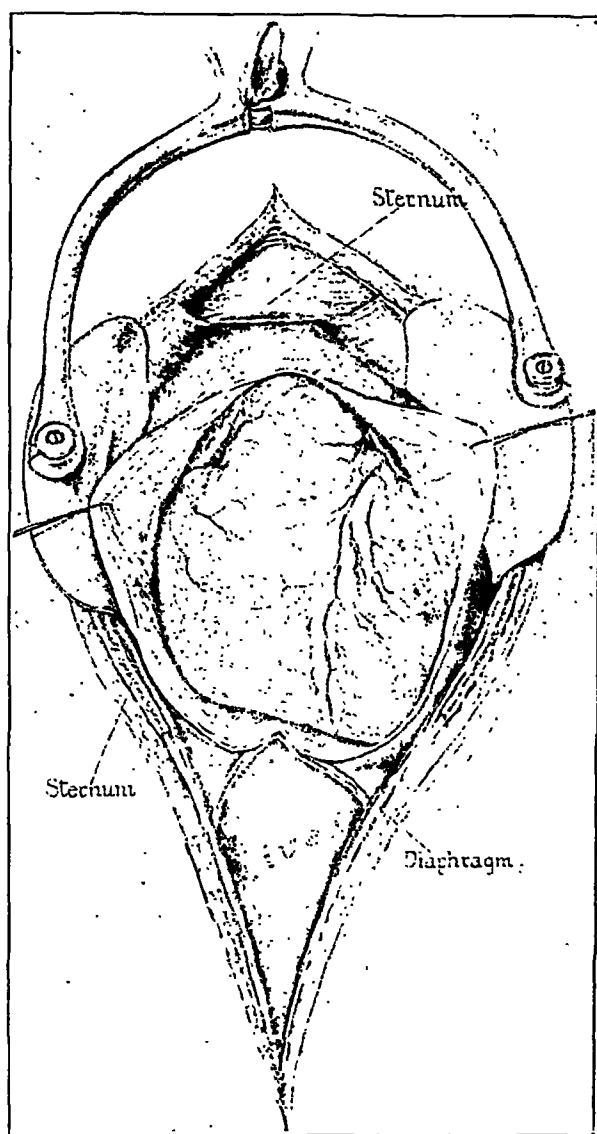


Fig. 3.—Exposure of heart by median sternotomy.

transversely. If the wound lies in the fifth interspace, the intercostal incision should be placed in the fifth rather than in the fourth interspace.

The method has its advantage in that exposure of the left pleural cavity is obtained. It is the method of preference in those cases accompanied by a wound in the left lung from which there is active bleeding.

2. METHODS OF SUTURE

What is encountered when the distended pericardium is opened depends on several conditions. If there was no active bleeding from the wound in the pericardium the bleeding from the wound in the heart may have subsided. Active bleeding from the wound in the pericardium

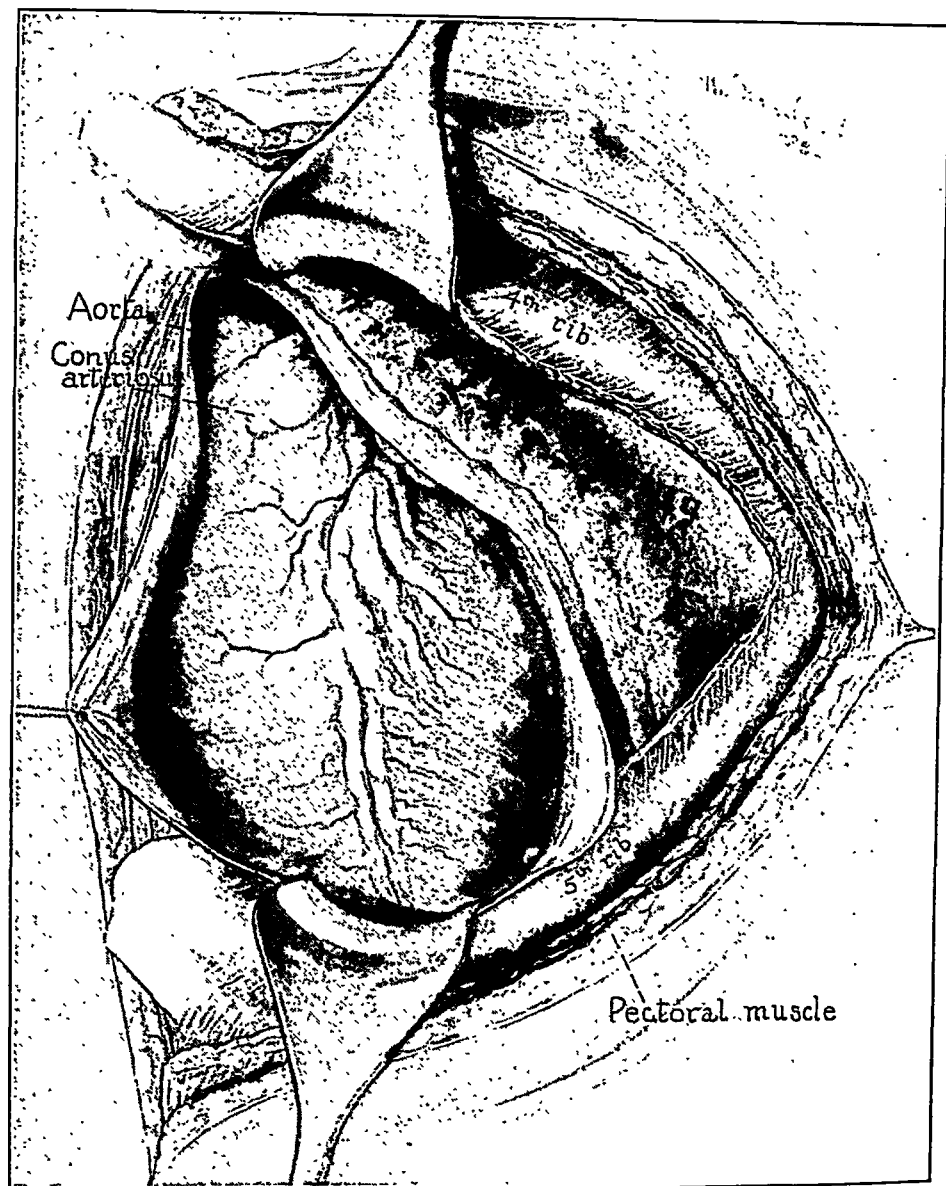


Fig. 4.—Exposure of heart by intercostochondral thoracotomy.

indicates active bleeding within. When the pericardium is opened and the tamponade relieved the heart usually undergoes several forceful contractions; the circulation is improved, and the patient may regain consciousness. The bleeding from a wound in the auricles, while it may be marked, depending on the extent of the wound, is continuous

and usually can be controlled without great difficulty if satisfactory exposure is obtained. If the wound enters the left ventricle or if a coronary artery is severed, the bleeding occurs in spurts that may strike the face of the operator. The following colorful description is given by Matas:⁵¹

More often the heart's action is violent and tumultuous, and the field of the operation is deluged with blood, which gushes out in intermittent streams, spouting sometimes beyond the wound in the thorax or folding up into a mass of froth which pours out of the external wound in large quantities. This is especially true of the cases complicated with a large opening in the pleura, which allows the air to rush in and out of the thorax with each respiratory movement and mix with the blood, the heart churning and lashing it into a thick crimson foam which entirely envelops the organ and hides it from the view of the operator. In these imposing circumstances it is impossible to see the wound, much less attempt to suture it. Sponging or mopping is worse than useless. There is but one alternative. The operator must then resolutely do one of two things: he must thrust his fingers into the pericardial sac through the swirl of blood and endeavor to locate the wound by palpating with his fingers and then plugging it with the finger-tips, if he finds it; or he must grasp the heart with his whole hand and drag the bleeding and writhing organ massively out to the thoracic wound, where, by gradually relaxing his grasp, the seat of the hemorrhage will be certainly identified and the suture can be readily applied.

Excluding those cases in which the bleeding is moderate and in which the wound can be sutured as easily as a wound in a striated muscle, there are, in general, two methods that have been utilized in the suture of cardiac wounds.

(a) *Compression of the Base of the Heart.*—A method for controlling hemorrhage from a wound in the heart by obstructing the flow of blood by compression of its base was proposed by Sauerbruch⁵² in 1907. With the right hand the apex of the heart is displaced anteriorly while the third finger of the left hand is inserted through the great transverse sinus,⁵³ and the fourth and fifth fingers are placed posteriorly in the pericardial cavity (fig. 5). Included between the third and fourth fingers are the venae cavae with a part of the right auricle and the pulmonary veins. By compression of these structures the flow of blood into the ventricles can be controlled. The thumb and

51. Matas, Rudolph: *Surgery of the Vascular System; Surgery, Its Principles and Practice*, edited by W. W. Keen and J. C. DaCosta, Philadelphia, W. B. Saunders Company, 5:67, 1909.

52. Sauerbruch, F.: *Die Verwendbarkeit des Unterdruckverfahrens bei der Herzchirurgie*, Arch. f. klin. Chir. 83:537, 1907.

53. The great transverse sinus in the adult is large enough to admit the surgeon's finger. This can be done without difficulty at operation if it is remembered that lying posterior to the aorta and pulmonary artery is a free passage from one side to the other.

index finger of the left hand are free to steady the heart while the wound is sutured (fig. 6).

It was found experimentally that the heart and the brain could tolerate ischemia for a limited period of time. This period of safety in the dog was one and one-half minutes;⁴⁰ in the cat, three minutes,⁵⁴ and in the rabbit, three and three-fourths minutes;⁵⁵ if the obstruction was continued beyond these limited periods, either the heart failed to recover its normal rhythm or signs of degeneration of the cortical cells

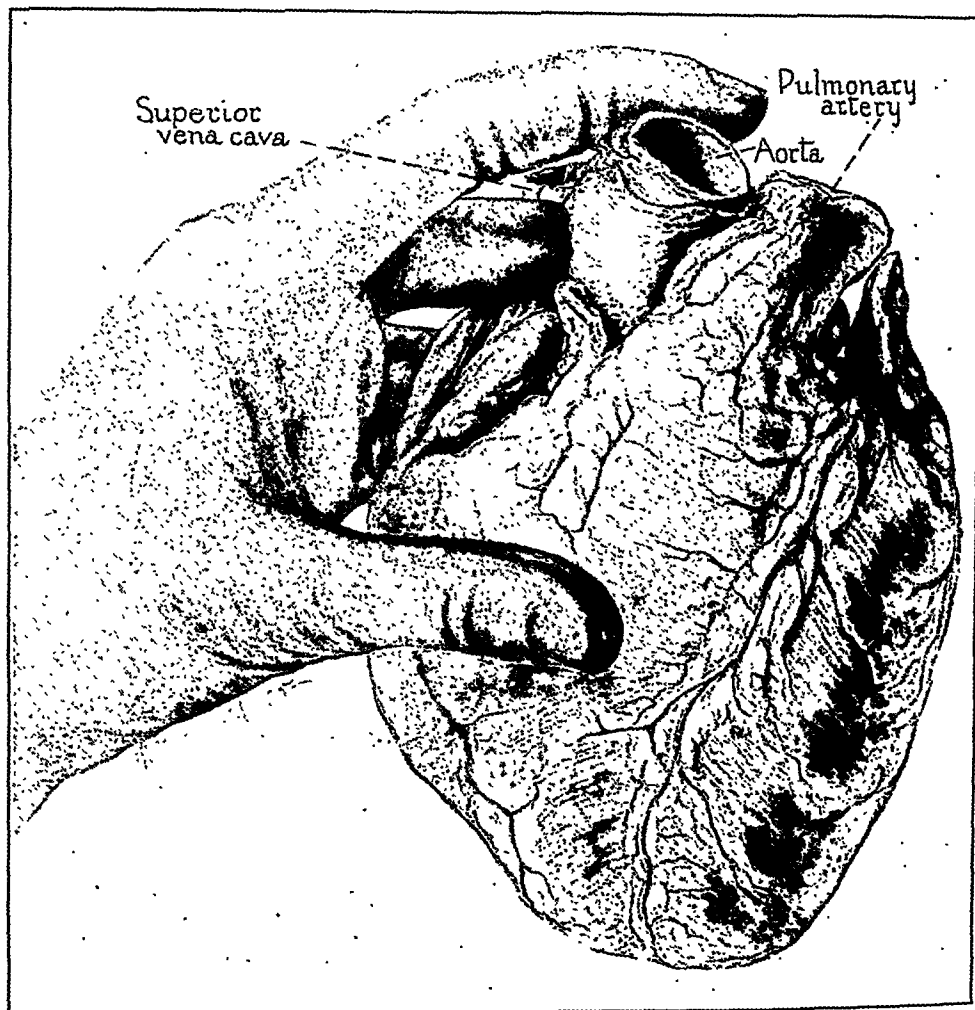


Fig. 5.—First step in method of controlling flow of blood through heart by compression of base: third finger is placed through great transverse sinus; fourth and fifth fingers are placed posteriorly in pericardial cavity; by compression with the fingers the venae cavae and the pulmonary veins can be occluded.

54. Cutler (Footnote 49, fourth reference).

55. Laewen, A., and Sievers, R.: Experimentelle untersuchungen über die chirurgisch wichtigen Abklemmungen des grossen gefässes in der Nähe des Herzens unter besonderer Berücksichtigung des Verhältnisse bei der Lungen embolie operation nach Trendelenberg, Deutsche Ztschr. f. Chir. 94:5, 1908.

developed subsequently. To prolong the period of safety it was suggested that intermittent or only partial obstruction to the flow of blood be effected during the process of suture.

From experiments on dogs Rehn⁴⁰ concluded that the method was not safe, but that in certain human cases its application was a necessity. That the ventricles themselves can be grasped forcibly in the hand of the operator and the wound sutured was shown in several successful human cases.

(b) *Plugging the Wound with the Fingers.*—To stop the bleeding by inserting the distal phalanx of one or of several fingers into the

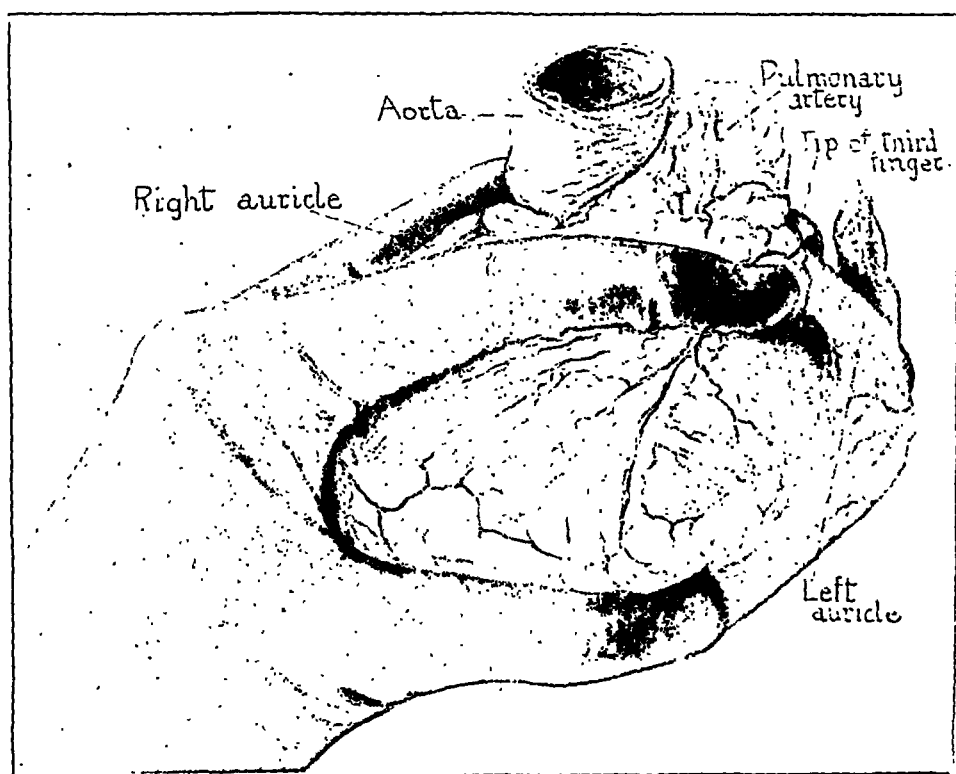


Fig. 6.—Second step in method of controlling flow of blood through heart by compression of base; the heart is steadied between the thumb and the index finger.

wound comes to the surgeon as a conditioned reflex. Moments are thus afforded in which one suture can be placed which, when tied on removal of the finger, helps to control the bleeding. Additional sutures, if necessary, can be placed.

3. DISPOSITION OF THE PERICARDIUM

The handling of the pericardium is an important factor in cardiac surgery. It may be involved in two serious operative sequelae: a

rapidly forming pericardial effusion, which may lead to fatal tamponade⁵⁶ and cardiopericardial adhesions, which commonly follow the subsidence of the effusion.

A study⁵⁷ of the factors concerned in these sequelae was carried out experimentally with the idea that they might be prevented or their serious consequences avoided. It was shown that operative trauma, infection, and the application of hot salt solution resulted in the formation of effusions and adhesions. The epicardium and parietal pericardium could scarcely be touched at operation without the subsequent formation of adhesions, and if an incision was made in the ventricle, a firm, dense adhesion to the pericardium almost always formed. Adhesions were not prevented by the transplantation of fat into the pericardium so that the incision in the ventricle came into contact with the transplant. The presence of blood in the pericardial cavity was of no consequence in the formation of adhesions.

That these sequelae might be avoided by pericardiectomy led to a study of the necessity of the pericardium for the normal function of the heart. Experimentally, the total or partial removal of the pericardium had no demonstrable effect on the general health of the dog, the response to exercise, or the size of the heart. The incised margin of the pericardium did not become intimately adherent to the heart.

It was concluded from this study⁵⁷ that compression of the heart developing as a sequel to operation could be avoided by incomplete closure of the pericardium without appreciable impairment to the functional capacity of the heart. As a precaution against tamponade an opening in the pericardium 1 or 2 cm. in length should be provided in every operation on the human heart. Because of the sensitivity of the pericardium to trauma the presence of a drain is not advisable. The heart should be delicately handled at operation and unnecessary sponging should be avoided. Rigid aseptic technic should be observed.

56. Rapidly forming postoperative pericardial effusions producing compression of the heart occurred in two cases in which operations were performed for mitral stenosis (Footnote 54). In one case the formation of the pericardial effusion was indicated by changes in the size and shape of the cardiopericardial roentgenogram. It assumed its greatest extent on the third day following the operation, having increased about 2 cm. in its transverse diameter. It then began to decrease in size and this was accompanied by an improvement in the condition of the patient. In the second case extensive fibrous adhesions between the heart and the pericardium were sectioned at operation. At operation the pericardium was closed throughout its entire extent. Toward the end of the postoperative period, which lasted about twenty hours, the patient presented the picture of a failing circulation. The postoperative roentgenogram showed an increase of 1 cm. in the transverse diameter. At necropsy 350 cc. of fluid was found in the pericardial cavity, the rapid formation of which undoubtedly produced a fatal tamponade.

57. Beck, C. S., and Moore, R. L.: *The Significance of the Pericardium in Relation to the Surgery of the Heart*, Arch. Surg. 11:550 (Oct.) 1924.

During the postoperative period signs of compression should be watched. Standardized roentgenograms,⁵⁸ which permit accurate comparison of the size and shape of the cardiopericardial shadow, are an important adjunct. If compression of the heart occurs pericardiotomy should be performed.

V. EXPERIMENTS

Methods of suturing wounds of the ventricles and of the auricles were tried experimentally on dogs. Under ether anesthesia the heart was stabbed with a long slender knife inserted through the chest and the pericardium, and the operation of suture was performed. The exposure of the heart under aseptic precautions required several minutes during which time variable amounts of bleeding occurred and variable degrees of tamponade were sustained.

It was found in general that wounds of the right ventricle were less difficult to control and suture than wounds of the left ventricle. The ease with which auricular wounds could be sutured depended on the exposure of the wound. If a satisfactory exposure could be provided, the wound could be closed readily with one or two Lembert sutures. In the discussion that follows reference is made only to wounds of the ventricles.

In these experiments it was found that compression of the heart during the process of suture, although capable of making the operative field bloodless, was poorly tolerated. Fibrillation, which in the dog was fatal, occurred in about half the experiments in which compression was used. Other factors in determining the result were the breed of dog⁵⁹ used, the degree of tamponade sustained by the heart, the extent of the wound, and the amount of blood lost.

The method of plugging the wound with the finger was utilized in several experiments in which stab wounds were made in the left ventricle. It was found that to control the bleeding by this method frequently

58. Successive roentgenograms can be standardized by having the chest recline at a constant angle, the roentgen-ray target placed at a fixed distance and at a constant angle posterior to the heart, and the plate at a fixed distance and at a constant angle anterior to the heart. For this purpose a special bed, an adjustable plate holder, and an adjustable frame to hold the roentgen-ray tube were used at this clinic. A sheet of canvas was used for the constant support of the chest instead of the ordinary mattress and spring so that it was unnecessary to move the patient in taking the roentgenograms.

59. A marked variation in the ability of the heart to withstand trauma existed in various breeds of dogs. This resistance to operative trauma was greatest in the bulldog and terrier, and least in the chowchow and hound. A simple incision in the left ventricle of the latter was sometimes fatal. The heart of the cat and of the rabbit was more resistant than that of the dog, and the heart of the goat was peculiarly capable of withstanding trauma better than any of the animals named. The human heart also has a high degree of resistance to the immediate effect of operative trauma.

called forth so much pressure on the finger that the cardiac muscle was torn, the wound accordingly enlarged, and the difficulties of the procedure augmented. In several experiments exsanguination occurred before the wound could be sutured. Furthermore, the presence of a finger in the wound added to the difficulty of placing a satisfactory suture. Because of its marked friability cardiac muscle could not withstand inclusion in clamps and forceps, and such instruments should not be applied.

Experience with the foregoing methods for the control of hemorrhage from wounds of the heart was afforded also in the experimental work carried out in conjunction with Dr. Elliott C. Cutler in the development of a method for the surgical relief of mitral stenosis.⁶⁰ In these experiments deliberate incisions were made in the left ventricle for the introduction of the cardiovalvulotome, and the unsatisfactory results of controlling these incisions by compression or by plugging with the finger led to the development of another method.

METHOD OF CONTROL SUTURES

When the pericardium is opened a suture to steady the heart is placed in the apex, the wound in the heart being momentarily disregarded. The impulse to control the bleeding instantly by placing a finger on the wound should not be heeded until the apex suture is placed. Unless the heart be steadied, the finger cannot be maintained in position. The apex suture is held under traction between the thumb and the third finger of the left hand, and the index finger is placed on the wound (fig. 7). The bleeding is thus controlled. The movements of the heart are transmitted to the left hand; both move in unison so that the index finger can be maintained effectively on the wound. This can be done regardless of its position on the ventricles. Two control sutures taking a deep bite of muscle are placed, one on each side of the finger at the level of the wound. They are crossed and then held under gentle traction by the assistant as the index finger is removed. The apex suture is dropped. An excellent exposure of the controlled wound is provided and ample time may be taken in placing the permanent sutures (fig. 8). Coronary vessels, if they lie adjacent to the wound, can be avoided in the sutures and a neat approximation can be obtained. The apex and the control sutures are removed.

The heat of the operation is over when the index finger is placed on the wound while the heart is steadied by a firm hold on the apex suture. If the idea be fixed in the operator's mind first to place a suture in the apex, disregarding the wound momentarily, the suture can be

60. Beck, C. S., and Cutler, E. C.: A Cardiovalvulotome, *J. Exper. Med.* 40: 375 (Sept.) 1924.

placed in a few seconds and the subsequent procedure becomes remarkably simple. The flow of blood through the heart is not interrupted and sufficient time may be taken to complete the procedure with deliberation. The operator should have noted the position of the wound under the finger so that the control sutures can be placed at the level of the wound. They should be placed also as near the margin of the wound as the

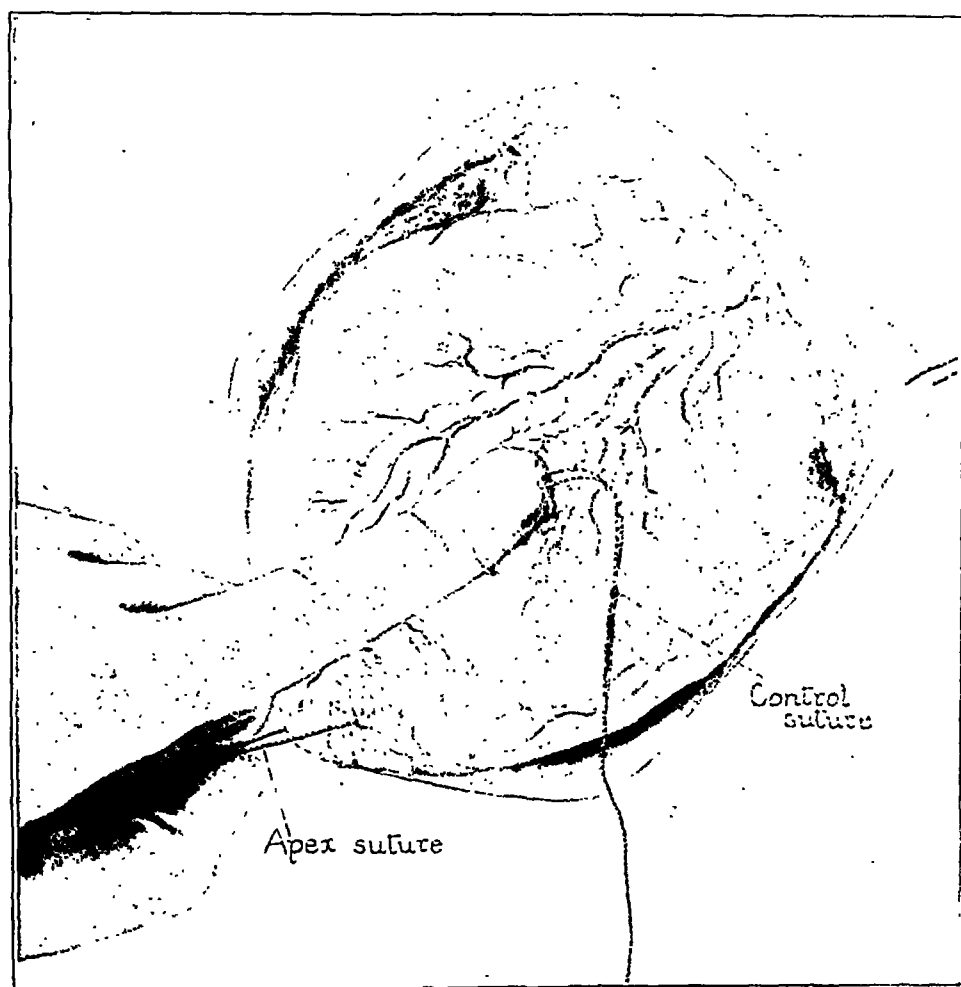


Fig. 7.—New method of suture: control of hemorrhage from wound preparatory to suture; traction on apex suture steadies heart so that index finger can be maintained effectively on wound; a control suture is being placed.

overlying finger allows. Traction on them is most advantageously applied when they are held by the assistant an inch (2.5 cm.) or two from the wound. The traction should not be so strong as to tear through the muscle. If it is found on removal of the index finger that the bleeding is not entirely controlled, the finger may be replaced on the wound and another control suture placed on each side at the point where

the bleeding occurred. The four control sutures, two from each side, are crossed and held by the assistant. In this way a wound of almost any size can be controlled, and a good exposure for placing the permanent sutures can be obtained.

The method was applied successfully in the suture of stab wounds made experimentally in the right or the left ventricle of the dog. It

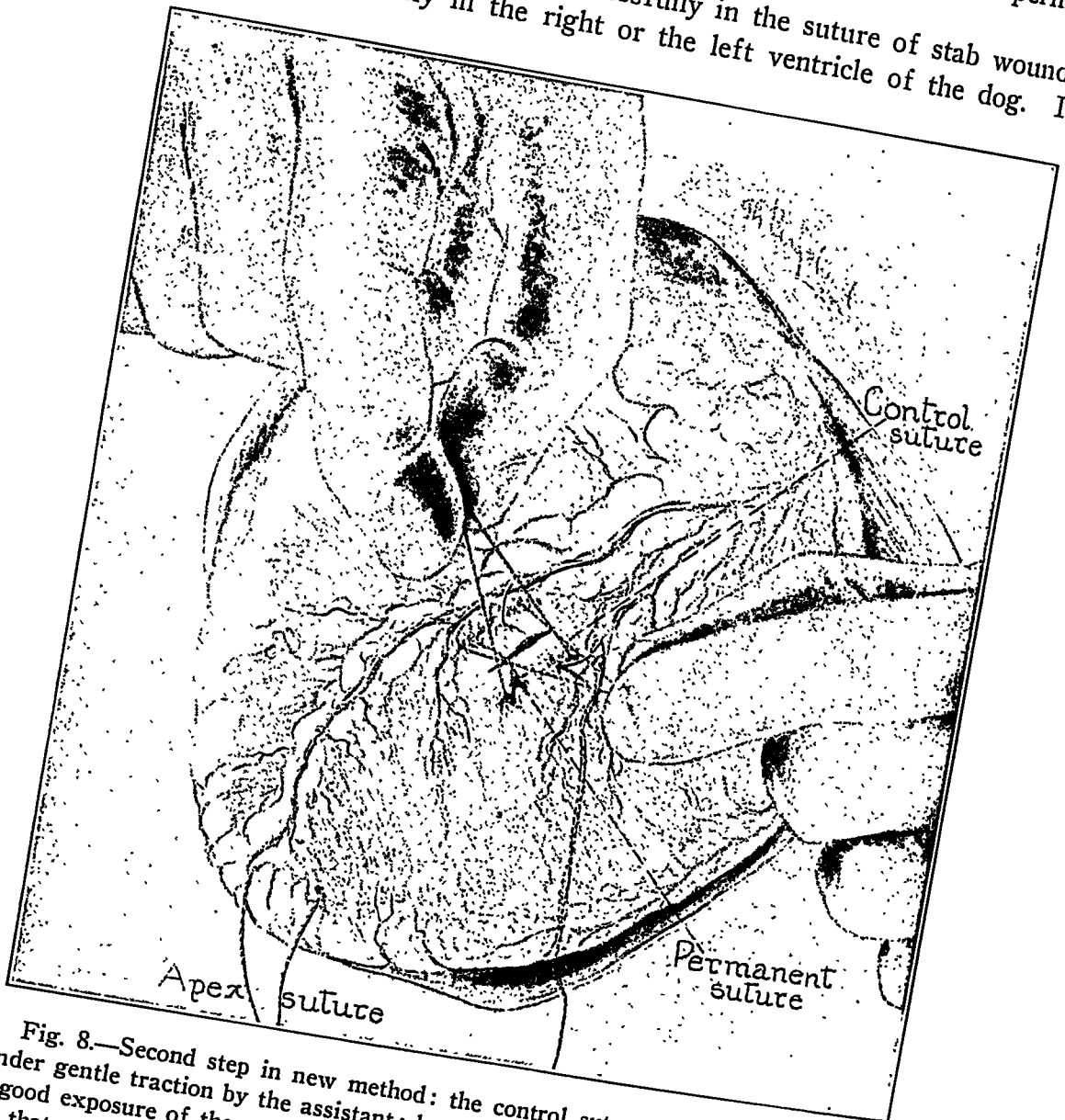


Fig. 8.—Second step in new method: the control sutures are crossed and held under gentle traction by the assistant; hemorrhage can thereby be controlled, and a good exposure of the wound is provided. The permanent sutures can be placed so that adjacent coronary vessels are avoided and a satisfactory approximation of the wound is obtained.

was the method of choice in the control and suture of the incision made in the left ventricle for the insertion of the cardiovalvulotome⁶⁰—an instrument devised for sectioning the mitral valve. It was entirely satisfactory in the control and suture of the incision made in the left

ventricle in two human cases in which operations were performed for the relief of mitral stenosis.

The method has its advantages in that the flow of blood through the coronary and the cerebral vessels is not occluded. It is well tolerated so that ample time may be taken to complete the procedure. An opportunity is afforded in placing the permanent sutures to avoid inclusion of adjacent coronary vessels. A neat approximation can be obtained.

THE MECHANISM OF BACTERIAL INFECTION

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This discussion will deal practically exclusively with infection produced by bacteria of the aerobic variety. I have little experience with the infections produced by anaerobic organisms except as these take part and are found in cases of intrapulmonary suppuration. The little I can say is that, clinically, established infection by anaerobic bacteria is usually produced by mixed infection with more than one organism; that the latter are probably originally secondary invaders and when centered in the foci of pulmonary suppuration are productive of slight or moderate grades of damage, and that when inoculated into a previously uninfected tissue, as happens after operations of the lobectomy type, the resulting pathologic change is extensive and of maximum intensity and results in death in 50 per cent. or more of the cases.

TERMINOLOGY

In medical literature the phenomena of bacterial infection are associated with the usage of the following terms: sepsis, sapremia, septicemia, bacteriemia, pyemia, general infection and general blood infection. Much confusion surrounds the use of these terms owing to the loose way in which they are generally employed. The term sepsis has sometimes wrongly been made to include the term sapremia; this inaccuracy should be avoided altogether. The term sepsis is a generic term and should include all forms of infection by virulent organisms capable, under appropriate conditions, of producing pus. In this sense typhoid infections, etc., are a form of sepsis as well as osteomyelitis, furuncles, carbuncles, etc. Under this definition, sepsis includes all septicemias, bacteriemias, pyemias and general blood infection as described here. The term general infection as it has lately been introduced in the literature is synonymous with sepsis.

Under ordinary conditions an infection is established by a certain type of organism and the course of the infection continues throughout with that organism as the sole cause. Quite commonly, however, the course of an infection is disturbed by an influx of organisms of a different type than those which are originally present. The differences are perceptible in the pathologic and clinical manifestations and are demonstrated in the bacteriologic studies. Added infections of this kind are known as secondary infections and the organisms as secondary invaders. They are particularly prevalent in infections in which wounds are exposed either during dressings or because of the types of treatment employed

(sunlight treatment, for instance); such secondary infections are frequently of no consequence in the clinical progress of the infection. In fatal cases secondary infection is very common just before death, and in these it sometimes assumes the clinical manifestations of a terminal general blood infection.

The two cases that follow are rather striking examples of secondary infection.

CASE 1.—A baby was vaccinated against smallpox in the usual way on the arm. The resulting lesion did not heal in the way these inoculations usually do; but instead grew larger and became more excavated, and the base of the ulcerated area became covered with a brown crust. Finally, the cause of this abnormality in the behavior of the vaccination was proved to be a secondary infection with diphtheria bacilli; these organisms were demonstrated in smears taken from the discharge from the ulcer. The patient promptly recovered after the proper administration of diphtheria antitoxin.

This case was published by Roosen Runge:

CASE 2.—A patient was admitted to the hospital with a left metapneumonic empyema. A blood cultivation made before operation was sterile. The pus in the chest contained pneumococci. Eight days after operation, physical signs of a right pleural exudate became evident. Two days later, the discharge from the operated empyema cavity became hemorrhagic. One day later, a blood cultivation demonstrated 30 colonies of diphtheria bacilli per cubic centimeter of blood cultivated. Cultures of the discharge and of the exudate from both sides showed diphtheria bacilli also. Two days thereafter the patient died. The postmortem examination showed an endocarditis and cultures made from the heart valves resulted in a growth of diphtheria bacilli also.

The term *sapremia* is understood to indicate a condition in which a focus of decomposition is present in the body the chemical products of which are absorbed into the blood and lymphatic circulations of the body and produce constitutional symptoms. The decomposition takes place in circumscribed tissue which having become dissociated from the rest of the body, as far as its biologic connections are concerned, becomes for practical purposes a foreign body; the most typical example of this is the retained placenta after childbirth. The bacteria giving rise to this decomposition belong to the saprophytic group of organisms and are characterized by their inability to invade living tissue as a part of, and in intimate relation with, the rest of the living body, that is, by a lack of virulence. Living organisms of this group are never found in the blood stream, not because they do not pass into the circulation but because the bacteria destroying powers of the host are always sufficiently active to cause their immediate disappearance.

The term *septicemia* implies a condition in which a local lesion is present owing to the invasion of a body tissue in intimate biologic connection with the rest of the body, by virulent bacteria. Poisonous toxic

bodies result from the growth of the organisms which, being absorbed into the body circulation, spread throughout the body and give rise to constitutional symptoms. Confusion exists in differentiating between cases in which bacteria can be demonstrated as being present in the blood and those in which they are absent, and the term septicemia has been loosely applied to both, especially when the histories of cases are given. The definition and use of the term has even been confounded with that of the term pyemia. The terms general blood infection or general infection, which have lately come into use, have been employed practically as an equivalent of septicemia, and have come to mean a bacterial infection of the body with or without demonstrable local lesions in which living organisms can be demonstrated to be present in the circulating blood by the usual cultural methods. According to some, septicemia is distinguished as a condition in which the organisms are multiplying in the blood circulation.

The term pyemia is an old one and a good deal of confusion has surrounded its usage and still does. If the term is to be employed at all it seems best to restrict its usage to infections of the body in which more than one lesion is present and in which it can be established that one of these is the original portal of entry for the infection, and that the others result from the transmission of the infecting agent from the latter or that all of the lesions are secondary to an obscure or demonstrable healed primary lesion. The original portal of entry is usually designated as the primary lesion; the other lesions are secondary, subsidiary or metastatic lesions to the primary focus. The term pyemia is used equally often in conditions in which bacteria are demonstrated to be present in the blood and in those in which they are absent, in cases in which there are few bacteria in the blood and in those in which the organisms are multiplying in the circulation; in these aspects the definition of the word is confused with that of septicemia.

It seems best to avoid the use of this confusing terminology and to make a much more simple classification of the phenomena of infection on the following basis; this will be employed here and in other articles.

1. The term infection will be used as a generic one and will include all of the phenomena of a bacterial attack on tissue, organ or the entire body. The various kinds of infection will naturally be described in accordance with the tissues, organ or part of the body involved, and in accordance with the organism or organisms encountered; thus, saprophytic infection of the uterus, staphylococcus infection of the skin, or streptococcus infection of the liver, etc. When no other modifying term is employed it is to be assumed that cultivations of the peripheral blood taken during life are sterile. The differentiation commonly made between local and general infection theoretically does not exist, and the

terminology is one more of convenience than of accuracy. Local infections must necessarily involve some degree of general constitutional reaction and general infections must necessarily find their beginnings in, or be associated with, a local focus of infection. As far as possible this differentiation will be avoided or made clear in the text whenever it must be used.

2. The term "bacteriemia" also will be used in a generic sense to indicate any condition in which bacteria can be cultivated from the peripheral blood during life. The various kinds of bacteriemia also will naturally be described in accordance with the organism found; thus staphylococcus bacteriemia, streptococcus bacteriemia, etc.

3. The term "general blood infection" will indicate a subgroup of the generic term bacteriemia and in this and in articles to follow a distinction will be made between the terms bacteriemia and general blood infection on the following basis: The term bacteriemia is meant to imply a condition in which the organisms demonstrable in the circulating blood by the usual cultural methods are derived from a local lesion somewhere in the body, are usually small in number, and the faculty of destroying the circulating bacteria is more or less retained by the appropriate antibodies of the blood. The term general blood infection is meant to imply a condition in which, in addition to the foregoing, a multiplication of the bacteria takes place in the circulation and the faculty of destroying the circulating bacteria is more or less lost by the appropriate antibodies of the blood.

Under appropriate circumstances both of these groups of terms will be employed together; thus, staphylococcus infection of the skin with staphylococcus bacteriemia or general blood infection. The character of the local lesion in the complete development of any individual infection is best described by the use of the terms primary or secondary (metastatic, subsidiary); thus, primary staphylococcus infection of the skin with staphylococcus bacteriemia, or primary streptococcus infection of the tonsil with secondary streptococcus infection of the appendix, etc., the absence of any descriptive bacteriemia indicating that a cultivation of the peripheral blood made during the course of the illness was sterile.

CLINICAL DISTINCTION

A distinction between cases of infection made on the basis of the presence or absence of living bacteria in the peripheral blood is clinically a most important one. Theoretically the distinction does not exist. It seems fair, from all the available evidence, to assume that in every case of infection, whether it be mild or severe, organisms are entering the circulation. In the cases in which cultivations of the peripheral blood made during life are sterile it should be assumed that the organisms

which reach the circulation are immediately destroyed in some way or other by the appropriate protective agencies. A bacteriemia or general blood infection exists only when the bacteria destroying agencies are partially or wholly lost, or inhibited. The bacteria destroying power may be lost or inhibited for only short periods of time and the bacteriemia accompanying such a state is spoken of as a temporary one.

In clinical practice infection of the human body appears in one of the following forms:

1. A local lesion is present apparently without any constitutional symptoms. This must necessarily mean that the amount of constitutional disturbance is so small as not to be perceptible to the affected person or recognizable to a competent examining physician. The best examples of this type are the small furuncles that occur on the back of the neck.

2. A local lesion is present with general constitutional symptoms. The latter show an infinite number of variations both in degree and in kind, and the manifestations may be very severe and may terminate in the death of the individual. Positive blood cultures are not demonstrable.

3. Cases similar to those in Group 2 but in which living organisms can be demonstrated in the circulating blood. The bacteriemia may or may not be a temporary phenomena; the organisms may be present in the blood in cases that go on to recovery and may disappear from the circulation in cases that later end fatally.

4. Cases in which secondary lesions appear. Living organisms may not be demonstrable in the circulating blood, or may be demonstrable as a temporary or permanent phenomenon; may be present in comparatively small or in overwhelming numbers; may be demonstrable in cases that go on to recovery, and may be absent during the entire course of the illness in cases that go on to a fatal termination.

5. Cases in which a bacteriemia exists but in which a local focus is not demonstrable. The term cryptogenetic sepsis has been applied to this form of infection but present day knowledge makes it advisable to abandon as misleading the use of this term. Under the last terminology cases of bacterial endocarditis had previously been included because a primary focus was not demonstrable.

As an explanation of the latter phenomenon—absence of a primary focus of infection—it has been assumed that it is possible for bacteria to pass through a body surface. For this purpose the surface of the body is not only the external skin but also the mucous membrane lining the entire extent of the alimentary canal, the entire lining membrane of the urogenital tract and of the pulmonary system. The epithelial lining of the ducts and the alveoli of all glandular structures in direct connection with any of these tracts is also an external surface of the body as

far as the introduction of infection is concerned. The conjunctiva of the eyes is also an external surface. This is but an extension of the universal law throughout living matter that no relation can exist between living matter and its environment except through its surface.

MECHANISM OF INFECTION

There is a continuous contact between the various surfaces of the body and bacteria of all kinds. It seems to be true that, even during states of health, traumas of one kind or another are constantly occurring to the major surfaces of the body—the skin or the intestinal mucosa—and that through these breaks bacteria of one kind or another are constantly entering the body. The protective forces of the body are, however, so well balanced, arranged and strongly developed that interaction of bacteria or of their biologic products and surface cells is prevented or, what is more often the case, the effects of this interaction are immediately neutralized and the bacteria that enter are immediately destroyed. No perceptible effect is demonstrable in the body cells, organs or tissues either immediately or subsequently, and the condition of health continues undisturbed. The balance between the attacking powers of the bacteria—their virulence—and the protective agencies of the body is a constant one during health.

PRESENCE OF TRAUMA

I am strongly of the opinion that the assumption sometimes made, that bacteria can pass through an intact healthy body surface, is an incorrect one. I believe, as far as the external skin and the mucosa of the alimentary canal are concerned, that no entry of bacteria can take place without the intervention of some trauma, however minute it may be. Even in the presence of trauma, it is only in extraordinary instances that the natural protection breaks down and disease ensues, either because the opposing bacterium is one of extraordinary virulence, or because the character of the infection is one to which the natural antibodies have previously, either in the individual himself or in his race, been not at all, or insufficiently, developed. Anthrax infection and the incidence of unaccustomed diseases in savage, aboriginal or other similar races make excellent examples of this point.

It seems much fairer to assume in cases of bacteriemia or general blood infection with obscure etiology that a primary lesion of some kind always exists. This may be in an inaccessible part of the body, *e. g.*, the folds of the intestines, where it can readily escape demonstration, or, if on an exposed and readily accessible location, it may have healed without leaving traces recognizable to the unaided eye before the subject came under observation; and having been of a most inconsequential nature and size, it had entirely escaped the notice of the person himself.

In any case, therefore, of such obscure forms of infections it should not be hastily assumed that a primary lesion did not exist, but rather that human deficiency is not capable of demonstrating the initial lesion in all cases.

In the deep tissues and in secondary lesions, trauma need not necessarily be a gross mechanical thing although, true enough, even here such trauma frequently exists and it is no uncommon thing in an established bacteriemia or general blood infection to witness abscesses form in the depths of a muscle or between the facial planes following a slight blow. Other forms of trauma are equally operative, chemical forms, thermal forms, etc. Any form of trauma produces either qualitative or quantitative inhibition of the vital cellular processes: (1) by actually destroying the molecular composition of the cells and with this their morphology; (2) by the development of chemical inhibitory bodies that inhibit or neutralize intracellular chemical reactions necessary in the life of the cell; (3) by deprivation of the normal food supply of the cells or tissues; (4) by favoring the accumulation of poisonous metabolic bodies; (5) by destroying fundamental physical cellular connections in cell groups accustomed to live together and dependent one on the other, leading in turn to disturbances in food supply, to abnormal accumulations of excrementitious matters, to incoordination, etc.

The most important mechanisms are mechanical trauma—even a strain or sprain is a sufficient trauma—and disturbances of nutrition of the cells. In trauma cells are exposed which are not prepared to withstand the attack of bacteria. In any case, trauma or lack of food supply, the actual result of the disturbance so far as infection is concerned is to produce tissue on which the bacteria can grow and in which bodies deleterious to the life of the bacteria cannot develop, or develop in such insufficient quantity as to be negligible. The most common mechanism for causing interference with the nutrition of the cells, organs or tissues is thrombosis and embolism, either of which by plugging a vessel deprives the intercepted territory of its main source of food supply. This will be gone into in detail in a later part of this article.

SURFACE INFECTIONS

Surface infections of the skin have intimate relations with the sweat glands and hair follicles, and obstruction to the outflow of any excretions from these passages is the most common immediate cause for the development of an infection. Surface infections of the intestinal tract have intimate relations with accumulations of lymphadenoid tissue. The most important of these are the tonsillar accumulations in the pharynx and those in the lower end of the ileum, Peyer's patches. Surface infections in glandular structures in connection with the alimentary canal, the liver,

pancreas, etc., are usually continuations of surface infections in the neighboring portion of the alimentary canal and are frequently associated with relative or absolute obstructions to the outflow of the gland secretions, such as are produced by the presence of stones or by spasm of the sphincter muscle at the outlet, produced by abrasions, etc. Surface infection at any junction of the skin and mucous membrane, e. g., the breast nipples or the anus, is most frequently, if not always, connected with trauma and the formation of fissures, which are especially prone to occur at this point because of mechanical trauma, such as suckling of the infant or passage of hard scybala.

Obstruction to the outflow of excretions of a glandular organ results in a damning back of secretions which in turn exerts an interference with the metabolic activity of the secreting cells. According to our definition previously given, this is a form of trauma.

Infection developed in any of these ways in a glandular organ can progress in one of two ways:

1. The infection remains centered in the gland lumina. A single abscess develops which when properly incised heals without any further progression of the inflammatory infectious process. In the breast this form is not as common as the second variety. The typical example of this form of infection in the liver is the amoebic abscess.

2. The development of the infection is communicated with the lymphatic channels and a typical form of lymphangitis develops. Multiple abscesses are the rule. This is the usual form of breast abscess, and in the liver it is the form usually seen with all types of infection except that caused by the ameba. It is possible for both of these forms of infection to coexist.

Infection of the urogenital tract is most frequently communicated by direct contact and is probably most often originated in minute traumas during intercourse. Progression of the infection occurs (1) by continuity along the surface; (2) through the lymphatics, and (3) by metastasis.

Infection of the pulmonary surface is most often associated with disturbances of the circulation, most frequently produced by chilling. With pneumococcus infections, progression of the process occurs by continuity along the surface; with certain other organisms penetration below the surface occurs and tissue becomes destroyed.

All these surface forms of infection are primary foci and in each case they act as portals of entry for the infecting organisms into the body system. Infection in a solid organ—such as bone or brain—or in tissue—such as muscle or connective tissue—not exposed on any surface of the body cannot be a primary affair, except in those instances in which excessive forms of trauma, such as compound fractures, lacerated, incise-

or punctured wounds, cause communications between the depths and the surface. Except for this, infections in such organs or tissues are metastatic affairs.

Infections of the body cavities, such as the peritoneum, the pleura or the meninges, are practically always continuations of infections in adjacent organs and are produced either by rupture of a hollow viscus, e. g., perforating appendicitis, or by continuation of the process through the lymphatics of the primarily affected organ, or by contiguity of an inflammatory process with the endothelial lining of the hollow cavity. In rare instances infection of these hollow cavities is metastatic. In women peritoneal infection can be a primary infection and frequently occurs by continuity through an open fallopian tube.

Absorption of bacterial toxins from any primary lesion occurs by way of the lymphatic system and by way of the blood stream. Penetration of the infecting bacteria into the body occurs also either through the lymphatic stream or through the blood stream. Both forms of communication are always necessarily present in all forms of infection. In certain classes of infection, especially those of the skin, and of the distal parts of the extremities, the preponderance of the lymphatic form gives rise to the typical clinical picture known as lymphangitis. In the latter form of infection the progression of the process from its portal of entry is a continuous one along the lymphatic channels, and the spread of the infecting bacteria into the body is a continuous penetration and growth along the lymphatic channels. Infections entering through accumulations of lymphadenoid tissue, notably the tonsils and Peyer's patches, are typical forms of lymphangitis as thus defined, and the progression of the infection along the lymphatic channels can be frequently demonstrated clinically in the secondary involvement by continuity of the regional lymph nodes in connection with these surface areas. In all forms of lymphangitis it is not possible to cultivate living organisms from the peripheral blood stream during the duration of the infection.

VENOUS THROMBOSIS

Communication of the infectious process and penetration of the infecting organisms from the portal of entry into the rest of the body by the blood stream is intimately associated with the subject of venous thrombosis. The inflammatory process associated with any infection has as one of its prominent characteristics the slowing of the blood stream and the formation of venous thrombosis. Under suitable circumstances the growth and multiplication of the bacteria in the focus of infection finally result in their penetration into the vascular channels, where in a relative way they are blocked from further progression, at least temporarily, by the occluding thrombus. However, the bacteria find an

excellent culture medium here, and unless their powers of further growth and development are destroyed by the natural forces of the body, they continue to multiply and to penetrate the clot until they reach the surface of the thrombus, where the bacteria come into contact with the freely circulating blood in a connecting channel. A number of possibilities develop as a result of this biologic progression:

1. The thrombi form a sufficient barricade and successfully localize the bacteria away from the circulating blood. Under such conditions no bacteria can be demonstrated in cultivations of the peripheral blood.

CASE 3.—A patient was given a transfusion during the course of a severe anemia. Following this the vein employed for entry became thrombosed and it was distinctly felt as a thickened cord at the bend of the elbow. This gradually became inflamed and an abscess formed. Healing followed promptly after incision and drainage of the latter. There were never any constitutional symptoms or other evidence to indicate that a bacteriemia was present, and cultivations of the peripheral blood remained sterile.

2. The growth of bacteria on the surface of the thrombus in contact with the circulating blood results in numbers of the bacteria being thrown off into the blood stream. The number¹ of organisms thus cast off into the circulation is relatively and actually small. In some cases the bacteria destroying powers of the blood are sufficient to kill the organisms as fast as they are thrown off, and in these cases positive blood cultures are not obtained. In other cases the bacteria destroying powers of the blood are only sufficient to kill the organisms a little less quickly than they are shed into the circulating blood. Positive blood cultures are then obtained but the number of organisms demonstrable in the peripheral blood remains small and the bacteria do not appreciably increase in numbers in successive blood cultivations. In practice recovery is possible from such forms of bacteriemia. The best examples of this are the milder bacteriemias associated with osteomyelitis and the cases of sinus thrombosis after middle ear infection with mastoid involvement.

CASE 4.—A patient had had a cholecystectomy done two years before admission. The healing of the wound was a most complicated affair and was marked by the development of an intra-abdominal abscess; for a time a fecal fistula also was present. Finally, healing took place and the patient was discharged from the hospital well.

Two weeks previous to the present admission the patient developed pain in the right side of the chest and a hacking cough; there was moderate fever and chilly sensations. Physical and roentgen-ray examinations demonstrated that there was considerable fluid in the pleural cavity and the aspirating needle showed that the fluid was pus. The usual thoracotomy was done and the chest was drained.

1. The number of organisms is estimated by making the blood cultivations according to the plate method. Each demonstrable colony corresponds to one organism in the circulating blood. The method is accurate for practical clinical work.

There was good immediate reaction; the temperature dropped and the amount of discharge was about what one ordinarily sees. Within several days, however, the discharge increased markedly and became foul; later it became distinctly fecal. The general condition of the patient deteriorated rapidly and for a while it looked as if a fatal issue was impending. Fortunately, however, this was temporary. The amount of discharge gradually lessened; the wound began to heal; the general condition progressively improved. Healing finally occurred and the patient was discharged well. This was probably a residual infection from the first operation two years ago and the suppurating focus worked its way through the diaphragm and into the thorax.

Coincident with the marked increase in the discharge and with its assuming a fecal nature, the temperature assumed an up and down course from 99 to 104 F., with daily remissions. There were numerous chills. At the end of the second week after operation and at the beginning of the third week, cultivations of the peripheral blood on several occasions showed small numbers of colonies of *Staphylococcus aureus*. A culture taken subsequently was sterile.

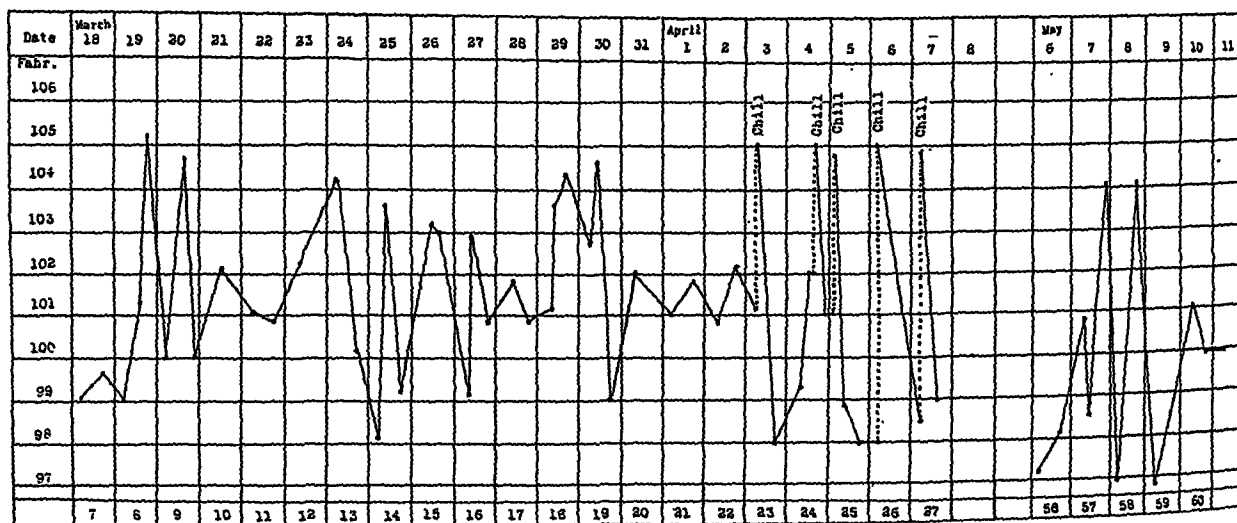


Fig. 1.—Temperature curve in Case 4.

The demonstration of a positive blood culture is explainable on the basis of the presence of an infected thrombus somewhere in the confines of the wound—possibly in an area of necrotic bone—which was in communication with the free circulation, so that organisms could readily find their way into the blood stream.

3. The growth of the bacteria on the surface of the clot in contact with the freely circulating blood is unhindered by any bacteria destroying powers and the organisms accumulate rapidly in the blood. In this form also the bacteria multiply in the blood stream itself. These cases are hyperacute forms of general blood infection and are almost invariably fatal. The commonest example of this is the fulminating form of general blood infection associated with severe forms of osteomyelitis and infections by the bacillus of anthrax.

CASE 5.—A child was first seen at the height of a fulminant acute infection with hyperpyrexia and a demonstrable focus in one clavicle. At operation the entire clavicle was excised in an attempt to remove the cause, the entire focus. The first cultivation of the peripheral blood showed 10 colonies of *Staphylococcus aureus* per cubic centimeter; one taken on the following day showed large numbers of colonies. Death occurred forty-eight hours after operation and the postmortem examination showed a widespread cellulitis of the neck and furuncles in the myocardium.

This case illustrates the usual course of affairs in a fulminant hyperacute case of infection with general blood infection.

These three descriptions do not portray distinct varieties of infection with and without bacteriemia. They indicate stages only in the development of the complete forms of general blood infection. The first passes into the second and then into the third. In clinical medicine

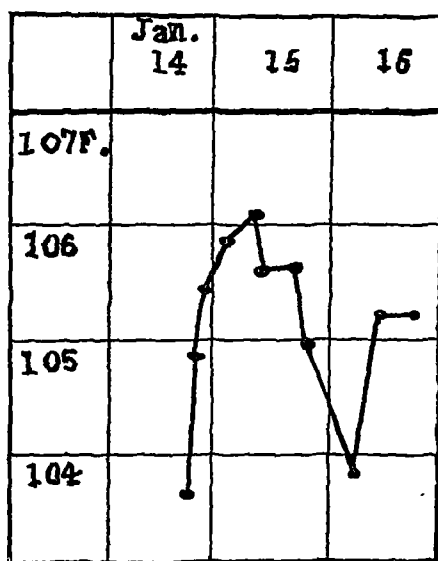


Fig. 2.—Temperature curve in Case 5.

and surgery regression is possible in any of the first two stages to complete recovery. Recovery from the third stage is apparently never seen. Cases that reach the third stage are uniformly fatal; cases in the other two stages may be fatal, especially when secondary lesions begin to form. Prognoses made during the first or second stage can be favorable with or without reservations; those made in the third stage must be unfavorable.

FORMATION OF SECONDARY FOCI

Under any of these three conditions the thrombi in the focus of infection contain living bacteria. Under any of these three conditions pieces of the original thrombus break off and are swept away in the circulation to all and any distant or near part of the body. Such

emboli form the cause of any and all secondary lesions. It is also possible for the bacteria alone floating in the circulation to become arrested at any point (for reasons which will be taken up in detail shortly) and to give rise to secondary lesions. Bacterial emboli, that is, clumps of agglutinated bacteria, also occur and act similarly.

The secondary foci are determined by the arresting of emboli at some point or points of the vascular network; these emboli are primarily, or become secondarily, infected. The actual point depends sometimes on an external trauma but more often on chance than on anything else and is decided by the physics of the local capillary circulation, or on the anatomic peculiarities of the local vascular network. Various pathologic pictures result, depending on the organ or tissue in which the embolus lodges, the size of the plugged vessel, the relative position of the plug, the facility and faculty for vascular anastomosis and collateral circulation in conjunction with the character and virulence of the organisms, and the general powers of resistance of the subject as a whole. Most typical pictures are obtained in osteomyelitis and in the metastatic furuncle of the lung. The dominant characteristics of the pathologic pictures of the secondary foci are (1) a thrombo-arteritis or thrombophlebitis, and (2) more or less necrosis consequent to disturbance of the local circulation. In certain tissues, such as bone, the necrosis plays a dominating rôle in determining the pathologic picture; in certain others, as in the lung, this is a negligible factor.

Sittmann reports the following case:

CASE 6.—A girl, aged 20, developed a prepatellar abscess; later this was complicated by an erysipelas. Eight days before death *Streptococcus hemolyticus* was demonstrated in the blood. After death, an examination of the body showed: (1) a right empyema; (2) a right axillary abscess; (3) periphlebitis and thrombosis of the axillary and jugular veins; (4) a paranephritis; (5) a parastrumitis, and (6) a suppurative arthritis of the left ankle.

It is most likely that the infected thrombus in the axillary and jugular veins gave rise to the bacteriemia.

CASE 7.—A patient was admitted to the hospital with the history typical of an acute attack of appendicitis; no previous attack had ever been present. Figure 3 shows a preparation of the appendix removed from this patient. The distal two-fifths of the appendix was totally gangrenous and there was a sharp line of demarcation between the gangrenous and the healthy portions of the specimen. The lesion was evidently a thrombo-embolic one. The appendicular vessels were first thoroughly irrigated in order to remove any contained blood, and it was noted that clear fluid escaped from the veins at the conclusion of the irrigation. The vessels were then distended with a solution impervious to the roentgen ray. Thereafter the appendix was fixed and finally cleared in essential oils. The preparation,² to the naked eye, shows the entire blood supply of the appendix, of which Figure 3 is an exact reproduction. The illustration

2. The specimen was prepared according to a method devised by Dr. Louis Gross. I am indebted to Dr. Harry Koster for Figure 3.

shows exactly where the blood supply was blocked. Collateral circulation is being established as shown by the fine anastomoses. This is a fine example of a secondary thrombo-embolic lesion during the course of an infection and illustrates the formation of a fixation point.

In any given environment of the body in which secondary foci may form, the anatomic arrangement of the vascular network can only be one of two:

1. In the one, more or less abundant provision is made for compensatory circulation around the arrested embolus. Under such circumstances the focus is quickly and sharply delimited and the extent of the resulting pathologic change is comparatively small; little or no necrosis occurs to increase the amount of destruction.

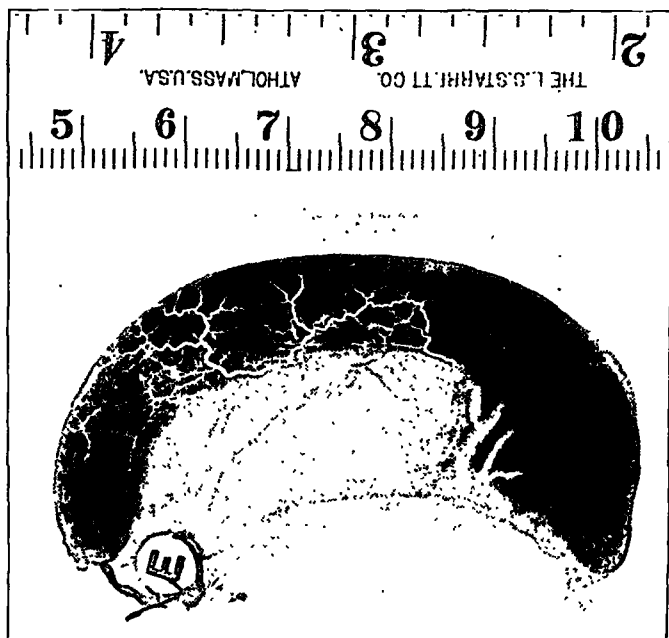


Fig. 3.—Newly formed bone, involucrum (shaded portion) around sequestrums, *A* and *B*; practically entire shaft was destroyed.

2. In the other, the provision for collateral and compensatory circulation is negligible or entirely absent around the arrested embolus. Maximum necrosis then takes place and the action of the bacteria in the embolus, their growth and spread into the necrotic tissue is unlimited; maximum destruction results. These forms are constantly occurring in clinical surgery and one need only indicate the gross characteristics of the pathology of a few as examples: the circumscribed furuncle of the lung, where abundance of circulation, compensatory and other, is the rule; the rapid necrosis and destruction of an entire diaphysis of a bone, in which the nutrient artery is plugged by an infected embolus and where compensatory circulation is negligible; the cutaneous petechiae;

etc. Each individual organ or tissue shows modifications of the pictures here described in accordance with its intrinsic structural peculiarities.

Figures 4 and 5 show the extent of variation in the faculty for collateral circulation and the relations of the latter to destruction of tissue. Figure 4 is a diagrammatic representation of secondary foci of infection in the lung observed postmortem. An attempt is made to show the relative proportions of the several foci and the rest of the lung. Figure 5 is a tracing taken of a roentgenogram in a case of osteomyelitis.

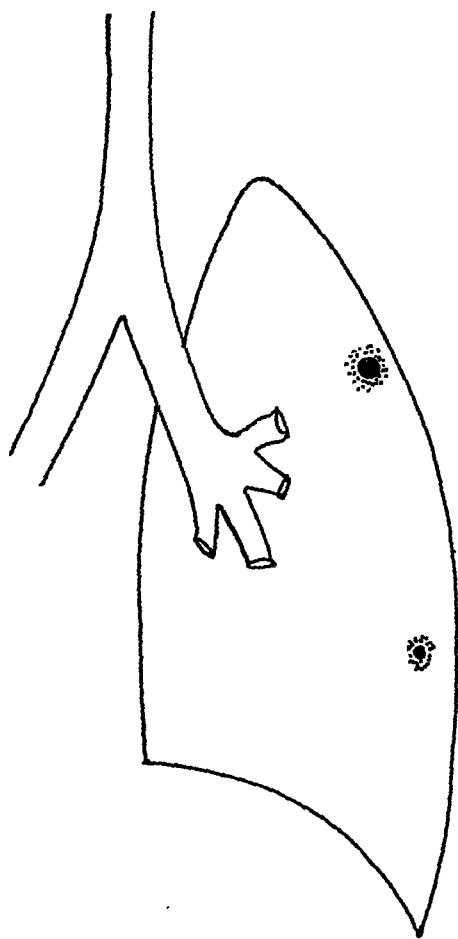


Fig. 4.—Diagrammatic representation of relative area of tissue involved in a territory well supplied with collateral circulation; comparison should be made with Figure 5.

Complete necrosis of the diaphysis eventually took place. The first of these two cases illustrates the minimum of destruction owing to abundant collateral circulation, and the second the maximum of destruction because the fixation point was in the nutrient artery and no collateral circulation was possible.

Comparison of these figures should be made with Figure 6, which shows an injection specimen of the liver. The picture reveals the

immensity and complexity of the vascular network of the liver. The possibilities present here for the formation of metastatic deposits should be considered and these possibilities compared with what one actually sees postmortem in cases of multiple liver abscesses of nonamebic origin. I am indebted to Dr. Gross for Figure 6.



Fig. 5.—Sketch from roentgenogram showing maximal amount of tissue necrosis which results when the thrombus-embolus formation is located in the nutrient artery of a bone and when little or no collateral circulation is possible; comparison should be made with Figure 4.

The physical characteristics of any secondary focus soon become similar to the primary lesion and vascular thromboses become important parts of the pathologic picture. All the characteristics of the primary lesion described here, as regards the presence or absence of bacteriemias

or general blood infections, and as regards the breaking off of secondary emboli and the formation of subsidiary foci, appertain just as readily to any secondary lesion, so that in actual practice any secondary lesion may in turn assume the characteristics of the primary lesion and become a secondary point of distribution for foci subsidiary to itself. The parallel continues to numerous or indefinite generations and the best example of the possibilities occurs in osteomyelitis with its numerous foci, occurring simultaneously or subsequently, in a short space of time or in periods extended over years in the same bone or in different bones.

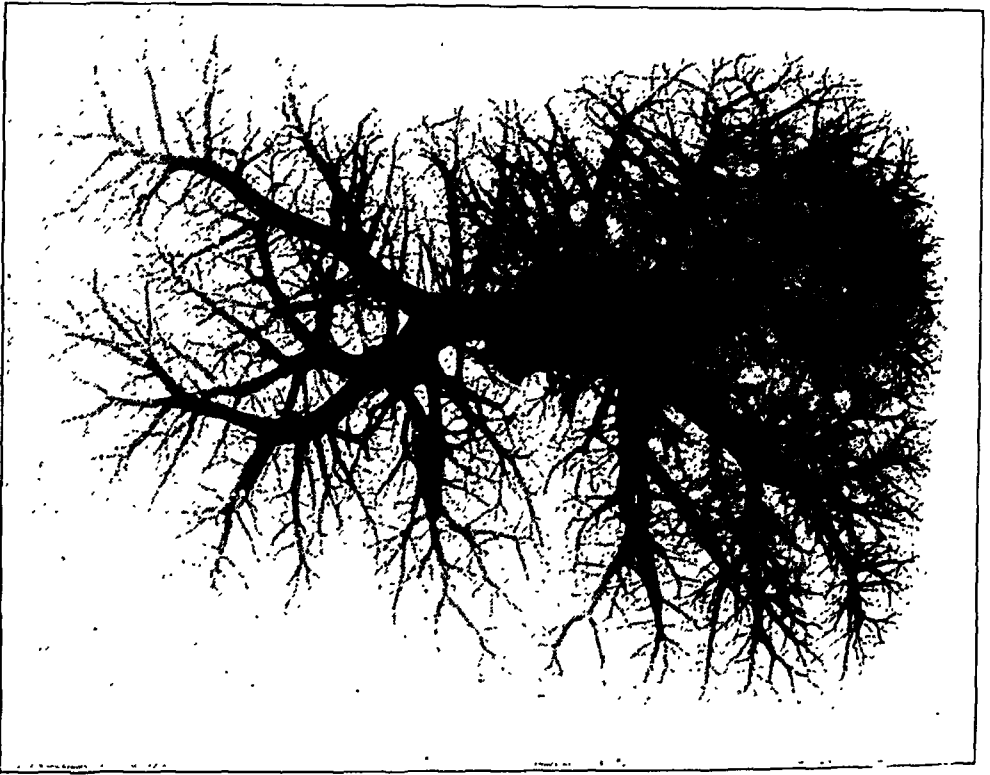


Fig. 6.—Injection specimen of liver described in text; courtesy of Dr. Louis Gross.

There is no experimental, clinical or other evidence nor any practical test that helps in classifying multiple foci developing during the course of an infection. It is perfectly possible for the primary lesion to form the origin for every secondary lesion that ever develops; and on the other hand, it is just as possible for any subsidiary focus, secondary or other, to in turn form a point of distribution and cause either some or all of the succeeding foci that subsequently develop. Sometimes it has seemed possible to distinguish the focus of distribution from purely clinical observation. Several foci are present and these are either in a healing state or have become healed. Subsequently the process relights in one of these and coincident with this exacerbation other new foci

develop. The fact that one of the older foci is in "active eruption" has made me feel that it in turn has become a point of distribution for the new ones.

CASE 8.—The notes of this case illustrate the difficulties in classifying the various lesions that can develop. Twelve days after the birth of a child and following the manual delivery of the placenta, chills and fever developed. Thereafter there developed in succession a femoral phlebitis, a pneumonia, an abscess of the leg and, last, an osteomyelitis of the upper end of the femur and an arthritis of the hip. Streptococci were the cause of the infection and the cultivations of the peripheral blood remained sterile. The relationships of the various foci that developed are subject to many possibilities.

CASE 9.—During the course of a pneumonia a femoral thrombophlebitis developed. After an initial subsidence of the symptoms and signs referable to the leg and during the convalescence of the pneumonia there was renewed activity in the femoral thrombophlebitis as evidenced by pain and fever. The patient died quite suddenly with well marked evidence of an intracranial embolism. Undoubtedly in this case the femoral and not the pulmonary focus was the point of distribution for the intracranial embolism.

PRESENCE OF BACTERIEMIA

A bacteriemia is not always demonstrable at the time a lesion is acting as a point of distribution and secondary and subsidiary foci appear when a bacteriemia is not present. Commonly this is so because the infecting bacteria are being transported in the emboli until they are caught and arrested at one or more fixation points, or, rarely, because the embolus was sterile; also, because the bacteriemia may have been a temporary one and the blood cultivation may have been made at a moment after the bacteriemia had disappeared or when bacteria were temporarily not present in the peripheral blood; whereas at other moments a blood cultivation, if made, would demonstrate the organisms. Technical errors on the part of the person making the blood cultivation may also be at fault.

CASE 10.—A patient was admitted with a fully developed follicular streptococcus tonsillitis and with the signs and symptoms of an acute lesion in the right iliac fossa. A gangrenous appendix, with considerable seropurulent peritoneal exudate from which streptococci were cultivated, was found at operation. The abdominal lesion was undoubtedly secondary to the tonsillitis, but the blood culture remained sterile. The patient recovered.

CASE 11.—A patient was operated on for inflamed gangrenous hemorrhoids. The usual excision operation was done, and it was noted that all the vessels were thrombosed. A low grade temperature developed. On the fourth day the patient became jaundiced and there was some slight tenderness over the liver. The primary lesion was in the thrombosed hemorrhoids and a secondary thromboembolic lesion of some kind developed in the liver. The blood culture was sterile. The liver lesion was apparently not very severe, probably owing to the small size of the embolus or the abundant collateral circulation of the liver. The patient recovered.

Temporary bacteriemias frequently occur after, and are caused by, the dressings of certain classes of wounds, especially those of bone, and are occasionally demonstrable.

In the following two cases it was possible to demonstrate temporary forms of bacteriemias which followed dressings of the wound.

CASE 12.—A patient had previously been operated on for multiple abscesses of the liver and during the course of his illness repeated blood cultures were entirely sterile, except for one on the forty-first day after operation. A blood cultivation of the peripheral blood had been made within an hour after the dressing and showed several colonies of *Staphylococcus aureus*. The sterility of the many blood cultivations made and the fact that previous experience had shown that liver abscesses do not give positive blood cultures go to show that the phenomenon was a temporary one and was due to the dressing of the wound (Fig. 8).

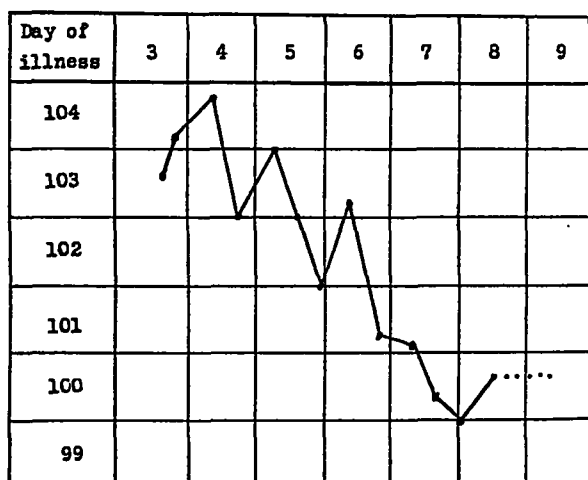


Fig. 7.—Temperature curve in Case 10.

CASE 13.—A patient had been operated on previously for an osteomyelitis of the femur. By the end of the second week the wound looked healthy; there were no other foci demonstrable; the fever was practically at the normal level, and there was no reason to suspect a bacteriemia. A blood cultivation, which was accidentally made within a short time after a dressing, showed several colonies of *Staphylococcus aureus*. This, too, was undoubtedly a temporary bacteriemia. Other blood cultures were uniformly negative.

CLASSIFICATION AS REGARDS BACTERIEMIA

In actual practice it is found that cases of infection can be of three kinds, as regards the presence of a bacteriemia:

1. In the first variety a focus of infection is present with well marked local signs and symptoms but without any clinical signs of a general blood infection. A bacteriemia is not present. The physical basis for this variety lies (a) in a primary and temporary bacteriemia; (b) in the

development of a fixation point, and (c) in the subsequent spontaneous disappearance of the bacteriemia.

2. In the second variety a well marked focus of infection is present with abundant local signs and symptoms and, in addition, there are clinical indications of a bacteriemia as evidenced by the general signs and symptoms and by the demonstration of living bacteria in the blood stream. The physical basis for this variety is the presence of an infected thrombus-embolus formation which serves to keep up a demonstrable bacteriemia by constantly feeding into the blood stream a comparatively small number of viable organisms. Commonly, after efficient surgical treatment, the bacteriemia eventually disappears and a recovery is made.

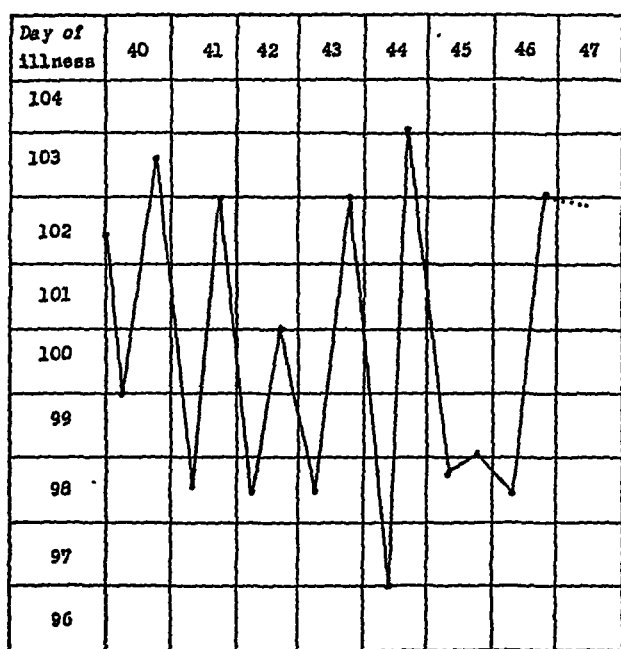


Fig. 8.—Temperature curve in Case 12.

It must be remembered that any of these cases may at any time pass into the third group. The possibility also exists, as mentioned in a preceding paragraph, of the local focus of infection in cases of this variety becoming a secondary point of distribution.

3. The clinical picture of the cases in this group is that of a profound general infection; there is a marked toxemia. A local focus of infection is either not demonstrable at all because of the paucity of local signs and symptoms, or because the latter are hidden in the profound intoxication, or, if present, the local lesion is easily recognized as being of no consequence in the total clinical picture. The physical basis of the picture lies in an extreme and severe general blood infection with highly virulent organisms in which the bacteria are rapidly multiplying in the

blood stream and because of which the subject is rapidly being overwhelmed by a tremendous intoxication. The presence of the infected thrombus-embolus formation forms a negligible factor and the few organisms that are derived from this source play only a primary and inciting part in the production of the bacteriemia; the subsequent multiplication in the blood stream depends on other factors, the most important of which lie in the high virulence of the infecting organism and in the poor resistance of the subject. An endocarditis is usually found under these conditions. In this variety the local point of fixation plays no rôle in the production of any part of the clinical picture. Usually the latter is not in an advanced stage at the time the lesion is exposed, either on the operating table, or, as more commonly happens, in the necropsy room.

In actual disease it seems certain that the cases differentiated in these three groups form progressive stages each from the next preceding

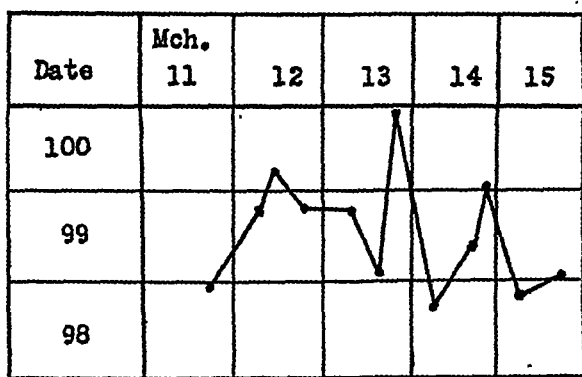


Fig. 9.—Temperature curve in Case 13.

group. A case in Group 1 may pass into Group 2; and, conversely, a case in Group 2, either because it had been appropriately treated, or spontaneously, may retrogress into Group 1 as it proceeds to healing and recovery. These interchanges are constantly occurring in clinical surgery. A case in Group 2 may pass into Group 3 as is previously noted; usually under such conditions there is a continued progression until the eventual fatality. In actual practice cases in Group 3 must necessarily first pass through the stage indicated by Group 2; the time interval may be so short, however, owing to the virulence of the infecting organism, as to be unrecognizable. One can explain the cases that apparently begin with the characteristics of the cases in Group 3 in this way. In many cases characteristics can be distinguished which belong to both Group 2 and Group 3; and so far as any case partakes of characteristics not belonging to its group, it differs in its clinical manifestations. I have never seen a case in Group 3 retrogress spontaneously into Group 2; it seems almost impossible to believe that such retrogression can ever occur.

From the facts stated here it becomes apparent that in any given case the presence of a bacteriemia must be referred: (1) to the primary lesion if this be present; (2) to any subsidiary lesion or to a number of them; (3) to the presence of a bacterial endocarditis, or (4) to a combination of these. In actual practice the relationship of the bacteriemia to the demonstrable lesions becomes an all important one and in certain cases valuable deductions can be drawn:

1. A single focus is apparently present in the presence of a bacteriemia in which comparatively small numbers of organisms are demonstrable in the peripheral blood. If, following an adequate operation in which the entire focus is removed, the bacteriemia disappears, it can properly be assumed that the bacteriemia resulted from that lesion. If, however, the bacteriemia persists after operation, and the surgeon is certain that the entire focus has been removed and the appearances of the resulting wound are healthy and corroborate this impression, the persistence of the bacteriemia may be used as evidence that some other focus exists which is causing the bacteriemia and which must be found and eradicated before the blood can become sterile and before cure can be affected. If, after a second focus is found and corrected, the bacteriemia still persists and the number of demonstrable organisms in the peripheral blood does not increase appreciably, indicating that the organisms are not multiplying in the circulation, a search for other foci must be made and a bacterial endocarditis must be excluded. The original focus should also be revised surgically. In the absence of these, the explanation of the bacteriemia becomes impossible for the moment even though it must necessarily be assumed that somewhere in the body an infected thrombus exists which is feeding bacteria into the circulation and which for the moment is not demonstrable. Prognoses under such conditions should always be made guardedly and with reservations, even though quite frequently eventual recovery ensues owing to the natural protective powers of the individual.

2. When several foci exist in the presence of a bacteriemia similar rules are followed and the explanation of the bacteriemia becomes a matter of exclusion.

3. In any case the relative numbers of bacteria demonstrable in the peripheral circulation in successive blood cultivations during the continued illness of the subject gives in appropriate cases valuable data for making prognoses: (a) Decreasing numbers of demonstrable organisms are associated with good prognosis. (b) Stationary numbers, when not too large, are associated with favorable prognoses, but with reservations. (c) When the numbers of bacteria are increasing, guarded prognoses should be given because the condition at the moment is a progressive one. (d) In the presence of large and overwhelming numbers of bacteria in

the peripheral blood, distinctly bad prognoses are indicated; usually the clinical picture is in accord with this. Increasing numbers of bacteria in the peripheral blood may diminish and disappear, especially if it is possible to eradicate completely the guilty foci. This is commonly seen in clinical practice. In the presence of bacterial multiplication in the blood stream, when large and overwhelming numbers are demonstrable in the peripheral blood, regression apparently is not possible.

4. In cases in which the bacteriemia continues in a comparatively unchanged condition in spite of all efforts, an endocarditis must be considered. The presence of a constant murmur—to be distinguished from anemic murmurs—should be taken as evidence that thrombi are present on the heart valves from which the bacteriemia is derived. The great majority of fatal cases of bacteriemia and general blood infection have this lesion at death among others.

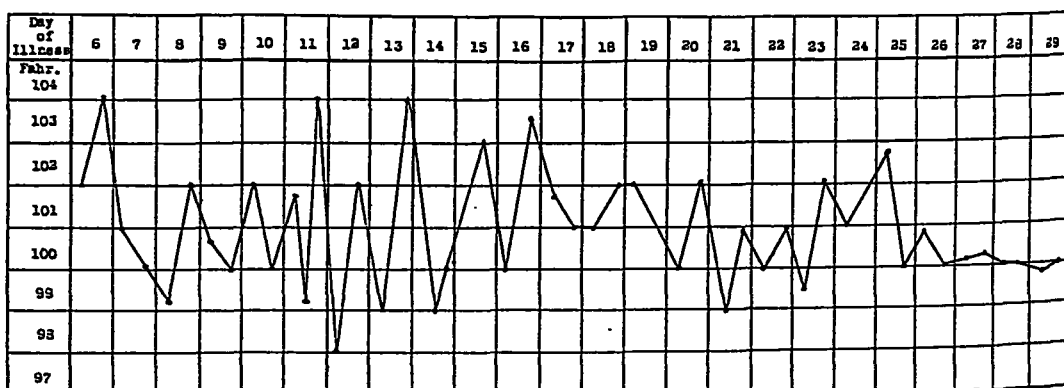


Fig. 10.—Temperature curve in Case 14.

CASE 14.—A young child was admitted to the hospital on the sixth day after the onset of an acute suppurative otitis media. The blood culture was sterile. There was apparently no mastoid involvement. On the fifteenth day, an arthritis of one ankle developed which was incised on the seventeenth day. On the twentieth day the blood cultivations showed one colony which on smear showed gram-positive cocci and a gram-negative bacillus. It was not possible for the pathologist, Dr. Gross, to identify these organisms. On the twenty-fourth day a focus developed in the left wrist and elbow, and on the twenty-fifth day the blood cultivation was sterile. The otologist, Dr. S. J. Kopetzky, suspected that a sinus thrombosis was present in association with the otitis media, but the physical signs and other evidence did not warrant any operative intervention. The child subsequently recovered.

This must have been a temporary bacteriemia of some sort. A good prognosis was always entertained and the impression proved correct.

I refer again to Case 2. In spite of the fact that the temperature and other constitutional symptoms continued during the time the bacteriemia was present, a guardedly favorable prognosis could be made. This was

possible because of the small number of bacteria in the circulation and because of the general condition of the patient.

CASE 15.—A young man developed an infection of the finger with high fever ten days before admission to the hospital. The temperature continued after the finger had been properly incised and two days later a carbuncle of the back of the thorax developed. Three days later the latter was incised. The temperature continued, however, and two days afterward the patient began to cough and brought up bloody sputum. On the day of admission, the eleventh of his illness, the physical examination showed a healing wound on the back and râles in both lungs, especially in their upper parts. The blood cultivation of the peripheral blood showed 190 colonies of *Staphylococcus aureus*. As shown in the chart, the number of colonies in the blood culture steadily declined until on the seventeenth day there were only 25 colonies per cubic centimeter of blood. Meanwhile the physical signs in the chest had increased until they were those of a confluent bronchopneumonia and the general condition of the patient remained fair.

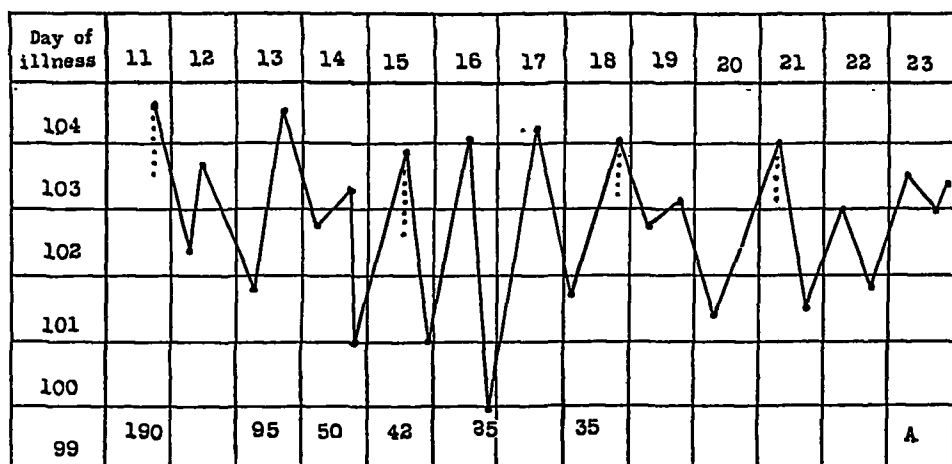


Fig. 11.—Temperature curve in Case 15; the figures represent the number of colonies of *Staphylococcus aureus*; A, numerous colonies.

During the last week of his illness the number of colonies again increased, the general condition deteriorated and the patient finally died.

During the first week the prognosis was certainly a most grave one but there seemed to be some hope from the continual improvement in the bacteriemia. The character of the physical signs and the general appearances of the patient contradicted this. In the last week all the available evidence seemed to indicate that a fatal issue would ensue.

CASE 16.—A patient was admitted to the hospital on the third day after he had been kicked in the knee. The admission temperature was 105 F. and the constitutional symptoms were those of a profound infection. An osteotomy was immediately done for an acute osteomyelitis. The bacteriologic studies showed *Staphylococcus aureus* in the pus from the bone and 25 colonies of the same organism in each cubic centimeter of blood. The after history suggested that the opening of the focus in the bone had no influence on the course of the illness, and death occurred four days later. Two days before death there were 150 colonies of *Staphylococcus aureus* per cubic centimeter of blood. The prognosis was bad from the time the patient was first seen.

CASE 17.—A young woman developed a malignant pustule of the face with high temperature. *Bacillus anthracis* was found in smears taken from the wound and the blood culture showed innumerable colonies of anthrax bacilli. This was a hyperacute general blood infection from the start. A bad prognosis was immediately made.

CASE 18.—A patient was admitted with a tonsillitis and high fever. The initial temperature subsided after the second day but returned the next day and steadily climbed to 105 F. Signs of a bronchopneumonia developed in one lung

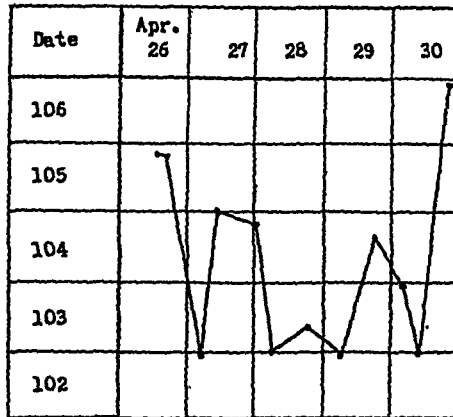


Fig. 12.—Temperature curve in Case 16.

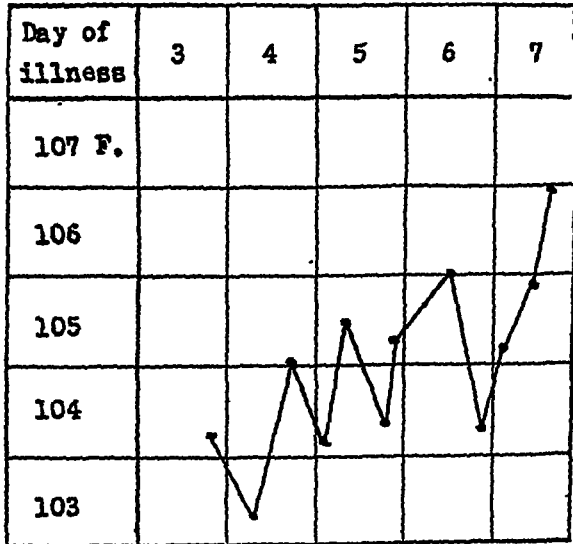


Fig. 13.—Temperature curve in Case 17.

and toward the end of the illness jaundice developed. The general appearances were those of a severe infection. A cultivation of the blood made on the seventh day of the illness and at the height of the temperature showed many colonies of a hemolytic streptococcus.

CASE 19.—A patient developed abdominal symptoms shortly after an acute tonsillitis. There were pain and cramps, most marked in the left lower abdominal quadrant, with some nausea and vomiting and a temperature of 103 F. The physical examination showed objective signs of a spreading peritonitis arising

from the pelvis. The vaginal and rectal examinations gave no positive findings. Laparotomy showed a diffuse peritonitis and spreads of the exudate showed pneumococci. The course of the illness was a progressive one and the temperature is shown in Figure 16. The blood culture was positive. The patient died.

There is room for a difference of opinion as to whether the portal of entry for the infection was the tonsil or the genital tract. The prognosis was bad from the time the patient was first seen. The peritonitis was a secondary focus of the infection and it is not possible to say whether the bacteriemia was referable to the primary or to the secondary lesion. A general blood infection (multiplication of the organisms in the blood stream) was present before death.

CASE 20.—A young girl developed a focus of infection in the general region of the right groin with general constitutional symptoms indicating a profound

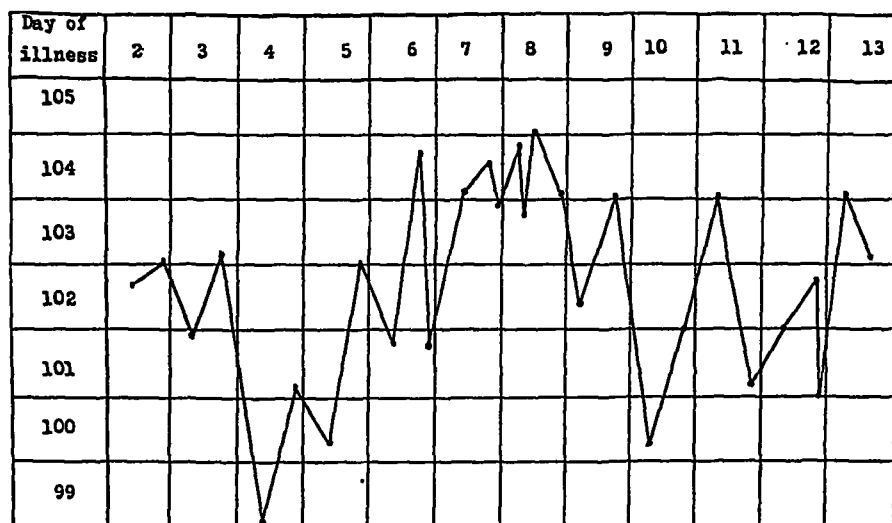


Fig. 14.—Temperature curve in Case 18.

infection. Operation showed that an infection had centered in the right hip joint, that the process had ruptured through the hip capsule, and that an abscess had formed outside the joint in the groin. Ample incision and drainage made no apparent effect on the signs and symptoms exhibited by the patient. The temperature curve up to the time of death is shown in Figure 17, and demonstrates the progressive nature of the disease. A cultivation of the peripheral blood made on the second day of the patient's stay in the hospital showed 20 colonies of nonhemolytic streptococci per cubic centimeter of blood. Five days later, two days after operation, there were fifty colonies of bacteria per cubic centimeter of blood; two days before death there were more than 100 colonies per cubic centimeter of blood. Pus from the joint and inguinal abscess showed non-hemolytic streptococci also. There was no postmortem examination.

It may be taken for granted that a focus of this kind is always a secondary one during the course of an infection. It was not possible, either from the history, the physical examination, or the subsequent

observation to determine the primary focus of the infection. This, too, was a progressively increasing infection and the patient was first seen in the stage in which a bacteriemia had already been established. The fact that the number of colonies demonstrated in the blood cultivations increased in the second blood examination gave great grounds for making

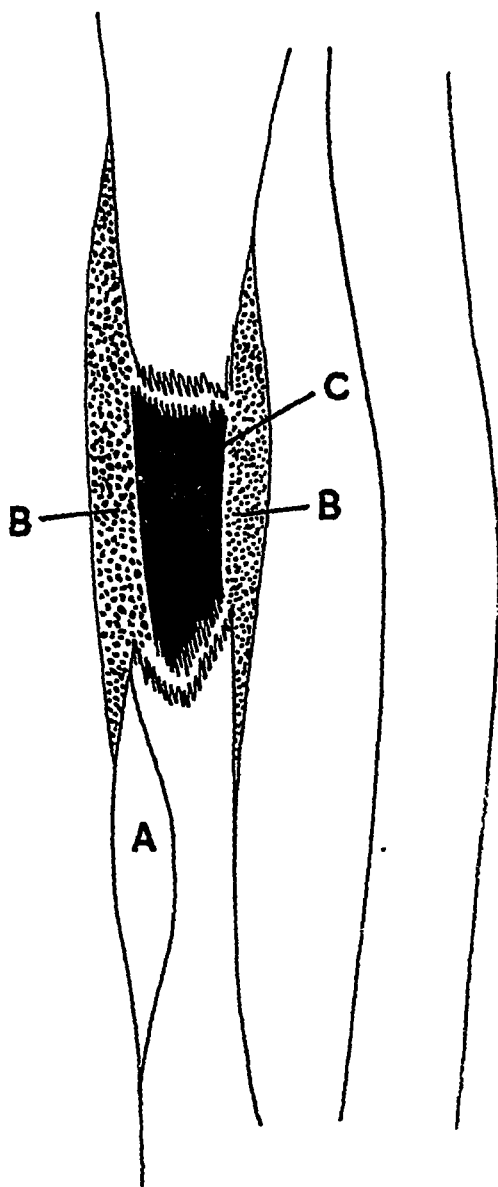


Fig. 15.—Sketch from roentgenogram in Case 19: *A*, primary osteotomy in radius; *C*, necrotic bone (sequestrum) which represents the spread of the focus at *A* by a spreading thrombosis, and *B*, involucrum around the sequestrum.

an unfavorable prognosis, and this was borne out by the clinical manifestations. There was a terminal general blood infection.

CASE 21.—On the ninth day after a radical operation for carcinoma of the breast, the temperature and other clinical manifestations indicated that everything was going well. On the tenth day, there was a sudden rise in temperature, as

indicated in Figure 18. On the subsequent days the temperature was high, remittent and was marked by daily chills. There was edematous swelling of the upper flap of the wound, where it overlay the axillary vein and the arm became swollen in the next twenty-four hours. There was no retention, or other abnormality in the wound, and no other cause, by physical examination and by roentgen ray, to account for the symptoms. The physical characteristics of the wound and the swelling of the arm indicated that the diagnosis was a thrombosis of the axillary vein. Cultivations of the peripheral blood were sterile at this time.

SIGNIFICANCE OF CHILLS

In many of the cases cited it is to be noted that there is a succession of rises and falls in the temperature curve interpolated by numerous

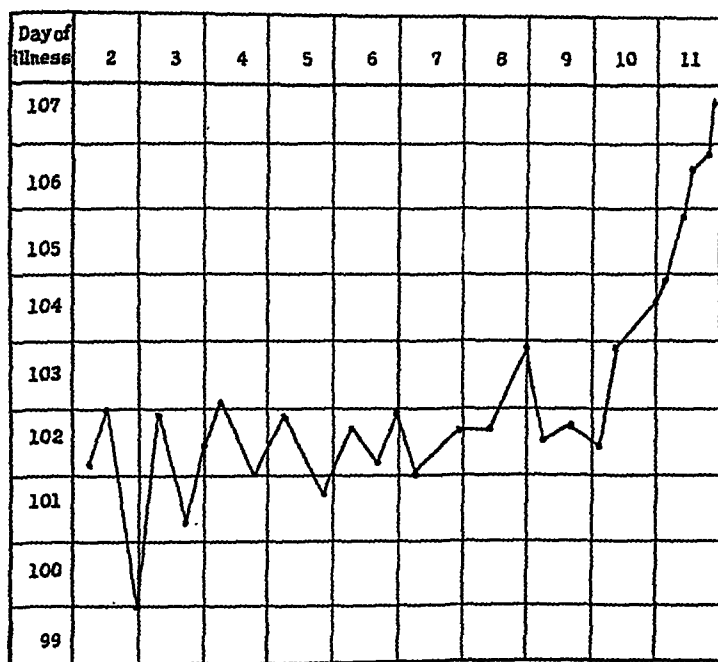


Fig. 16.—Temperature curve in Case 19.

chills. Such a temperature curve is always to be associated with bacterial thrombophlebitis in which the pathologic process is in an active stage and in which emboli are constantly being detached from the mother thrombus. Each of the chills and its subsequent rise of temperature corresponds to the breaking off of one or more parts of the thrombus and their discharge into the circulation as emboli, and with a sudden flooding of the circulation with organisms. The question whether these organisms are immediately destroyed completely or partially or are not interfered with at all, and whether the organisms so discharged into the circulation then proceed to multiply, is one that is intimately concerned with the bacteria destroying properties of the blood and, to an equal extent, with the virulence of the bacterial poisons set free in the

blood stream. The differentiation between bacteriemia and general blood infection, as previously defined in this article, and the occurrence of sterile blood cultures depends on the various relations of these all important general factors and the relative dominance of any one over any and all others.

The presence of chills in Case 21 indicated that this was not a quiescent thrombosis but an active one and that pieces of the thrombus had continued to be broken off at various times. The impossibility of demonstrating bacteria in the peripheral circulation indicated that the bacteria destroying powers of the blood were sufficient at this time to kill the bacteria as fast as they entered the circulation.

The question of prognosis was an important one at this stage of the illness. The general condition of the patient continued undisturbed and except for the fact that there were these daily rises of temperature and

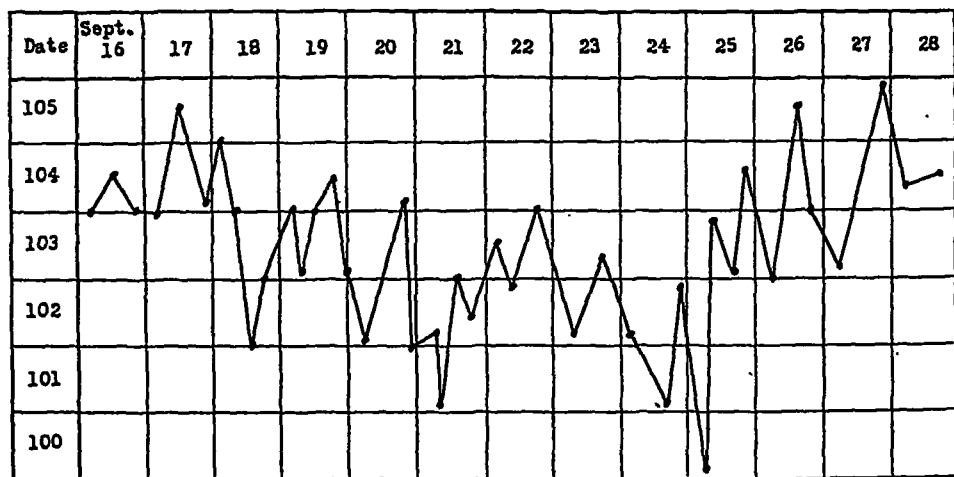


Fig. 17.—Temperature curve in Case 20.

repetitions of the chills, which incommoded the patient only while they lasted, there were no subjective or objective general manifestations indicative of the grave condition present. The condition of the wound continued as described. In clinical surgery such abnormalities of behavior occur after operation and usually these are only of temporary significance and disappear subsequently. The fact that a negative blood culture was obtained also was encouraging. A carefully guarded, favorable prognosis was, therefore, made at this time.

To continue the subsequent history:

During the fourteenth, fifteenth and sixteenth days after operation the daily level of the temperature showed a gradual decline. This was not coincident with any marked difference in the local conditions of the wound or in the general clinical manifestations. At this time we were much encouraged.

On the seventeenth day the temperature rose again and during the succeeding night and on the next day the chills were repeated. On the eighteenth day

the patient vomited for the first time. The general condition of the patient was still good. After continuing for two days the temperature again fell to 101.1 F. only to rise again to 104 F. on the same day. On the twenty-second day a subcutaneous abscess was discovered at one side of the scar and this was incised immediately. The incision and drainage, however, made no change in any of the clinical manifestations and from this time on, the temperature continued at a high level.

On the twenty-fifth day, there developed a persistent abdominal distention with nausea and continual vomiting of small amounts of bilious material. The bowels moved freely and the evacuations were of a diarrheal nature. The abdomen was soft in spite of its distention and was entirely free of pain, rigidity or tenderness. Nevertheless, I felt sure that a secondary lesion was going on in the abdominal cavity which I assumed was some form of a peritonitis.

A blood cultivation of the peripheral blood made on this day showed 26 colonies of hemolytic streptococci per cubic centimeter of blood. An abdominal

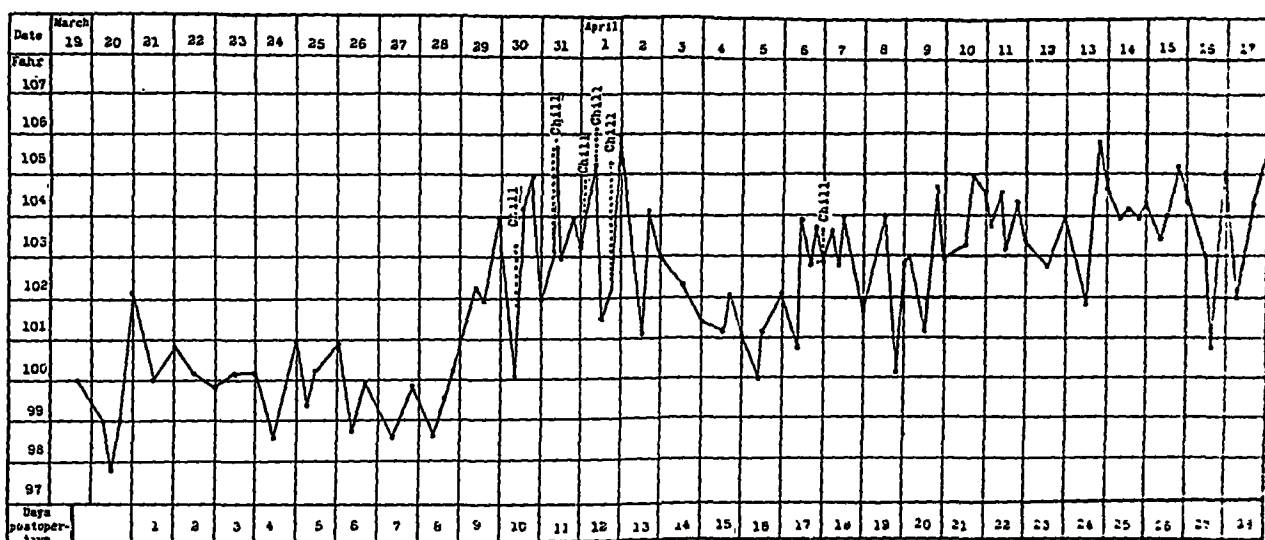


Fig. 18.—Temperature curve in Case 21.

aspiration was done and a few cubic centimeters of turbid fluid was obtained from the right flank. This was reported by Dr. Bernstein as containing no pus cells or bacteria on smear and as being bacteriologically sterile on culture. The patient's general condition began to deteriorate on this day.

The development of a secondary focus and the presence of a bacteriemia corroborated our assumption that a thrombophlebitis was present in one of the veins in the operated territory, most probably the axillary vein. The presence of the bacteriemia demonstrated that the resisting powers of the patient were flagging and that the organisms had established their position in the blood stream. From the relatively small number of organisms demonstrable, it was not possible to distinguish whether any multiplication of organisms was taking place in the circulation and whether enough natural protection still remained to keep the

number of organisms down to a low level. Probably some degree of multiplication must have taken place.

The laboratory data proved disturbing to the assumption that a peritonitis was present. The physical findings were suggestive and subsequently the continuance of the abdominal distention, of the nausea and of the frequent vomiting were seemingly not explainable except on that basis. At no time could we distinguish a pulmonary lesion to which abdominal distention might be a secondary manifestation, and on several days we could elicit the physical signs of ascites.

About this time the patient began to be drowsy. On the twenty-seventh day after operation the patient was deeply drowsy and could be aroused only with much effort. The general condition of the patient was poorer. There was increasing rigidity of the neck and a well developed Kernig's sign. In the evening the patient seemed stuporous.

On the twenty-eight day after operation all the symptoms had progressed and the diagnosis of meningitis seemed certain. This was corroborated by a lumbar puncture which released from the cerebrospinal space a few cubic centimeters of clear fluid in which Dr. D. J. Kaliski found 161 cells per cubic centimeter of which 88 per cent. were polymorphonuclear cells, and numbers of streptococci.

The infection of the meninges also was a secondary focus in the course of the infection. There were two possibilities: (1) that the meningeal focus was subsidiary to the primary lesion in the operative field; or (2) that the meningeal lesion was subsidiary to the secondary focus, whatever that might eventually prove to be, within the abdominal cavity. There were no data of any kind to help in making the decision and this question remained in doubt.

The development of this subsidiary focus, of course, removed any likelihood of the recovery of the patient and from this time on we looked for a fatality.

We resorted to several methods in the hope of removing the bacteriemia. A transfusion of blood was given to the patient. There was no time, of course, to give blood from an immunized donor. There was no apparent benefit following the transfusion. Full doses of gentian violet were given intravenously on several days. Except for a temporary fall in the temperature following the first of these, these injections also were followed by no apparent benefit. All of the signs and symptoms continued to increase progressively and on the twenty-ninth day after operation the patient died.

A postmortem examination of the body was made by Dr. Friedman. The notes of this are as follows:

The operative wound was in good condition. The axillary vein contained a thrombus in the region underlying the clavicle. This lay rather loosely in the lumen of the vein, was not obturating and was apparently unattached. The wall of the vein was apparently intact. There was a fresh bacterial endocarditis

with perforation of the valve cusps. There was an obturating thrombus in the terminal portion of the ileocolic artery. There was no peritonitis. There was no pneumonia.

This case is a most illuminating one and illustrates many of the points brought out in this article. The original point of entry for the infection was in the stump of one of the branches of the axillary vein in the operative field; because of some obscure factor, the thrombus which normally should occlude a ligatured vessel up to the point of junction with the next larger branch—in this case, the axillary vein—continued into the lumen of the latter; this made the mother thrombus. When this grew large enough, it presumably broke away from its point of attachment in the stump of the relatively small ligatured branch. Pieces of the mother thrombus breaking off and circulating through the vascular network of the body gave rise to the other lesions and foci detailed in the report of the case. Each accident of this kind, i. e., separation of one or of a shower of emboli, was marked clinically by a chill and a subsequent rise of temperature. As soon as bacteria began to grow on the surface of the various thrombi and emboli, bacteria began to appear in the circulating blood and were demonstrable in the cultivations of the peripheral blood. Later, the positive blood cultures were most probably due to the valvular lesion.

The presence of the abdominal distention, nausea and vomiting was finally explained by the presence of the embolic thrombus in the ileocolic artery. The interference with blood supply was undoubtedly much less than at the beginning; this corresponds with some diminution of the clinical symptoms referable to the abdomen in the terminal part of the illness.

Vascular thrombosis in a focus of infection acts as an important factor in delimiting the size of the lesion and in explaining its gradual or sudden enlargement. Thromboses that do not increase are associated with foci that remain stationary and undergo healing. Thromboses extending by contiguity along the vascular pathways are associated with lesions that increase in size. A similar spread of a focus of infection can also be secured by penetration of the bacteria along the lymphatic channels. Sudden increase of the thrombotic process, as, for instance, when a vascular bifurcation is reached or when a main nutrient vessel is reached explains the apparently sudden exacerbations that sometimes take place in foci of infection that are apparently doing well, and the sudden appearance of bacteriemia, or of general blood infection. In certain organs and tissues, notably bone, it explains the many obscure manifestations that are constantly being seen as regards the difference in the size of the initial focus and its immediate partial regression when collateral circulation is established, and of many

phenomena which are constantly occurring and which are difficult of explanation on other bases.

CASE 19.—The notes of this case illustrate how impossible it would be to explain the clinical phenomena except on the spread of the thrombo-embolic process. A young girl was operated on for a focus of osteomyelitis in one radius. A radical osteotomy was immediately done and thereafter the wound did well. At a subsequent dressing the appearances of the wound were those to enable one to strap the lips of the wound together with the expectation of an immediate agglutination; this occurred and about ten days later it appeared that the wound had practically healed. The patient returned several days later with a recrudescence in the arm and a roentgenogram (Fig. 5) showed something that appeared at first sight as a new focus close to the old one. This, however, was in reality a spreading of the original focus by retrograde thrombosis until a large trunk vessel had been reached in which the extension of the thrombosis and the spread of the infection had caused the involvement of another area of the same bone and the formation of a sequestrum.

Subsidiary foci of infection have often been termed fixation points on the supposition that, when such a secondary focus forms, it attracts to itself any bacteria that are present in the circulation and renders the latter sterile. This is true in the sense that the embolus that originates the subsidiary focus is the only part of the primary thrombus that carries the organisms from which the bacteriemia is derived, and that when the embolus is caught at its fixation point and properly blocked off by thromboses around itself no further discharge of bacteria can occur, at least temporarily. It is still possible for a bacteriemia or general blood infection to be derived from the primary thrombus at the original portal of entry of the infection or from others of its emboli that are being discharged either simultaneously or subsequently to the formation of the fixation point. In actual practice the bacteriemia does or does not disappear in accordance with the physical characteristics of the mechanism as here described.

This assumption is also true in the sense that sterile portions of a thrombus may form sterile emboli which, becoming caught at some point of the vascular network, form fixation points for the subsequent localization of any bacteria or bacterial emboli that may penetrate the circulation.

DISPOSAL OF BACTERIA ON RECOVERY

The ultimate fate of the bacteria in a case of infection from which recovery is made is a manifold one:

1. The organisms are taken up by the various protective cells, antibodies and fluids of the body until dissolution of them occurs.
2. Organisms are extruded and cast off from any operative or traumatic wound that is present.

3. Organisms that reach the liver disappear in their passage through the liver. In this regard it is known that certain classes of organisms are dissolved by bile.

4. Organisms are excreted from the intestinal tract, as in typhoid fever.

5. Organisms are excreted in the urine. In passing through and out of the urinary tract, the bacteria may leave no trace of their presence, or may cause surface infection of the lining epithelial membrane under proper conditions. The various other forms of nephritis or nephrosis that occur during an infection are due to the same thrombo-embolic phenomena previously described and to extension along the lymphatics of the kidney.

6. Small groups of organisms are isolated in the granulations of the healing wound and become encysted in the resulting scar tissue, or become encysted in organized thrombi. Sometimes as in typhoid bone infections they form sources from which subsequent secondary infections arise.

SODIUM CHLORIDE METABOLISM IN CUTANEOUS BURNS AND ITS POSSIBLE SIGNIFICANCE FOR A RATIONAL THERAPY*

EDWARD C. DAVIDSON, M.D.

DETROIT

The disturbance of fluid balance following extensive cutaneous burns is a well known phenomenon. Even though the fluid intake is relatively great during the first twenty-four hours, there is a marked urinary suppression. The normal ratio between fluid intake and output usually does not become established before the end of from forty-eight to seventy-two hours. During this period, the urine is deeply colored, has a high specific gravity, and may contain a trace of albumin. In view of this apparent suppression of the renal function and the fact that sodium chloride is badly tolerated by kidneys showing irritative lesions, it seemed desirable to study the sodium chloride metabolism and its relation to protein metabolism.

A number of observers have investigated the nitrogen metabolism in extensive burns. Robertson and Boyd¹ found that the nonprotein nitrogen of the blood was increased from 40 to 50 per cent in rabbits following burns. This was largely due to a relative increase of urea nitrogen, which constituted from 80 to 90 per cent of the total non-protein nitrogen as is usually the case in rapid nitrogen retention. They attributed this rise to increased protein catabolism. Underhill and his associates² observed a similar elevation of the blood nonprotein nitrogen and urea nitrogen, but thought it due to blood concentration. Davidson³ reported a suggestive parallelism between the blood nonprotein nitrogen and the clinical condition of the patient.

The chlorides of the blood in the normal person are relatively constant. Gettler and Baker⁴ state that the normal whole blood chlorides vary from 450 to 500 mg., while the plasma chlorides, calculated as sodium chloride, vary from 560 to 640 mg. per hundred cubic centi-

* From the surgical service of the Henry Ford Hospital.

1. Robertson, B., and Boyd, G. L.: *Toxemia of Severe Superficial Burns*, J. Lab. & Clin. Med. 9:1-14 (Oct.) 1923.

2. Underhill, F. P.; Carrington, G. L.; Kapsinow, R., and Pack, G. T.: *Blood Concentration Changes in Extensive Superficial Burns and Their Significance for Systemic Treatment*, Arch. Int. Med. 32:31-49 (July) 1923.

3. Davidson, E. C.: *Tannic Acid in the Treatment of Burns*, Surg. Gynec. Obst. 41:202-221 (Aug.) 1925.

4. Gettler, A. O., and Baker, W.: *Chemical and Physical Analysis of Blood in Thirty Normal Cases*, J. Biol. Chem. 25:211-222 (June) 1916.

meters. McLean and Van Slyke⁵ place the normal chlorides of whole blood at 490 mg. per hundred cubic centimeters and the normal plasma chlorides at from 597 to 614 mg.

The only recorded blood chloride observations in burned persons are those by Underhill² made in conjunction with studies on blood concentration. He did not record any urine examinations and the blood chlorides were determined for a maximum of three days. In a number of cases only one specimen of blood was analyzed. A lowering of blood chlorides was observed and was explained on the basis of blood concentration in response to the local inflammatory reaction and the pouring out of plasma on the skin surface. He concluded that in the rapid interchange of fluid during the inflammatory stage of burns the sodium chloride functioned prominently.

METHOD

Patients were placed on a diet⁶ that consisted of approximately 60 Gm. of protein with sufficient fat and carbohydrate to give a total caloric value of about 2,500 calories. The sodium chloride content of the diet was approximately 9 Gm. The amount refused was weighed and the total ingested food calculated. Fluids were forced energetically. The twenty-four hour intake of fluid was measured and the total urine collected. Periods ended at 7 a. m. when the patient was requested to void so that the division into day periods would be as accurate as possible. A specimen of blood was taken at this time. Heparin was generally used as the anticoagulant but occasionally sodium oxalate was employed.

The whole blood chloride values were determined in all instances by the Whitehorn method.⁷ In the case detailed in table 3, the whole blood chlorides and plasma chlorides were determined by both the Whitehorn and Van Slyke⁸ methods, to ascertain whether chloride could be bound with protein. The blood was collected and centrifugalized under oil and the analysis was done immediately to prevent any appreciable change in the plasma chlorides⁹ due to a shift of chlorides between plasma and corpuscles. Plasma volumes were determined by centrifugalizing the whole blood for twenty minutes at 2,500 revolutions per

5. McLean, F. C., and Van Slyke, D. D.: A Method for the Determination of Chlorides in Small Amounts of Body Fluids, *J. Biol. Chem.* **21**:361-370, 1915.

6. Locke, E. A.: *Food Values*, New York, D. Appleton & Co., 1920.

7. Whitehorn, J. C.: System of Blood Analysis, *J. Biol. Chem.* **45**:449-460 (Feb.) 1921.

8. Van Slyke, D. D.: The Determination of Chlorides in Blood and Tissues, *J. Biol. Chem.* **58**:523-529 (Dec.) 1923.

9. McLean, F. C.: The Numerical Laws Governing the Rate of Excretion of Urea and Chlorides in Man, I, An Index of Urea Excretion and the Normal Excretion of Urea and Chlorides, *J. Exper. Med.* **22**:212-216, 1915.

minute. The nonprotein nitrogen was determined by the method of Folin and Wu¹⁰ and the carbon dioxide combining power by the method of Van Slyke.¹¹ For the total nitrogen in the urine Folin's method was used, and for the chlorides the Whitehorn method.

RESULTS: MINOR BURNS

No alterations were found in either the blood or the urine chlorides in a group of seven cases of minor burns in which the lesions were not extensive and little tissue was actually devitalized, but in which the thermal agent was of sufficient intensity to cause a marked local edema. In table 1 are shown the results in a person who was burned to the first degree over the entire face and neck. There were a few small blebs over this area and the dorsum of each hand revealed a second degree burn. In this instance there was a normal chloride output in the urine and neither the whole blood nor the plasma chlorides revealed any striking change.

TABLE 1.—*Blood and Urinary Chlorides in Patient (Case 1) with First Degree Burn of Face and Second Degree Burn of Hands*

| Date | Fluids | | Diet | Blood | | | | | |
|------|---------------------|---------------------|-------|----------------------------|---|---|------------------------------------|---------------------------------|--------------------------------------|
| | In- take, Cc. | Out- put, Cc. | | Sodium Chloride, Gm. | Sodium Chloride Whole Blood 100 Cc., Mg. | Sodium Chloride Plasma 100 Cc., Mg. | Red Blood Cells, per Cmm. | Hemo- globin, per Cent | Urine: Sodium Chloride, Gm. |
| | | | | | Calo- ries | | | | |
| 8/30 | 5,400 | | 2,593 | 5.5 | 450 | 624 | 4,970,000 | 116 | 2.4 |
| 8/31 | 5,550 | 1,580 | 2,656 | 8.2 | 470 | ... | 4,920,000 | 108 | 10.5 |
| 9/ 1 | 2,804 | 2,980 | 2,601 | 9.00 | 462 | 619 | | 104 | 8.60 |
| 9/ 2 | 4,290 | 2,920 | 2,487 | 7.1 | 462 | 599 | 4,080,000 | 94 | 9.64 |
| 9/ 3 | 5,660 | 3,420 | 2,633 | 8.4 | 462 | 588 | | ... | 10.44 |
| 9/ 4 | 3,920 | 2,460 | 2,341 | 6.7 | 462 | 569 | 4,250,000 | 90 | 6.09 |

MODERATE BURNS

A group of twelve patients with burns of somewhat greater extent and severity were observed showing second or third degree burns that involved a cutaneous area of somewhat less than 1,000 sq. cm. In general there was a transient but definite disturbance of chloride metabolism. The values for the blood chlorides fell but promptly returned to normal, while the urine revealed a mild, temporary chloride suppression. In figure 1 are shown the curves of the whole blood chlorides of the individual cases as well as the average curve for the group. An initial fall is noted with a secondary rise to normal limits, the latter taking place on about the fifth or sixth day.

10. Folin, O.: Laboratory Manual of Biological Chemistry, New York, D. Appleton & Co., 1922.

11. Van Slyke, D. D.: A Method for the Determination of Carbon Dioxide and Carbonates in Solution, J. Biol. Chem. 30:347-368 (June) 1917.

TABLE 2.—Blood and Urinary Chlorides in Patient (Case 5) with Second Degree Burn of Left Leg

| Date | Fluids | | Diet | | Urine | | Blood | | | | | | | |
|---------|----------------|----------------|----------|-----------------------|----------------------------|-----------------------|----------------------------|--|--|---|---|----------------------------------|---------------------------------|------------------------------------|
| | Intake, Cc. | Output, Cc. | Calories | Nitro- gen, Gm. | Sodium Chloride, Gm. | Nitro- gen, Gm. | Sodium Chloride, Gm. | Non- protein Nitrogen per 100 Cc., Mg. | Sodium Chloride Whole Blood per 100 Cc., Mg. | Sodium Chloride Plasma per 100 Cc., Mg. | Carbon Dioxide Combining Power, per Cent by Volume | Plasma Volume, per Cent | Hemo- globin, per Cent | Red Blood Cells, per Cmm. |
| 8/18/25 | 5,100 | 5,050 | | ... | ... | 2.2 | 0.51 | 33.3 | 300 | ... | 58.7 | ... | 86 | 4,250,000 |
| 8/19/25 | 5,025 | 4,000 | 989 | 3.4 | 2.1 | 28.0 | 2.3 | 37.0 | 370 | 553 | 58.4 | 54.4 | 87 | 4,270,000 |
| 8/20/25 | 5,725 | 2,750 | 1,026 | 0.8 | 7.0 | 19.4 | 1.6 | 40.0 | 421 | 628 | 51.4 | 56.0 | .. | |
| 8/21/25 | 4,340 | 1,800 | 2,400 | 9.4 | 8.3 | 23.3 | 0.7 | 20.0 | 478 | 619 | 55.3 | 62.9 | .. | |
| 8/22/25 | 8,095 | 1,800 | 2,188 | 0.1 | 0.0 | | | 38.5 | 437 | ... | 53.7 | 57.0 | .. | 4,020,000 |
| | | | | | | | | | | | | | | 3,650,000 |

In table 2 are shown the results in a case of second degree burn of the left leg below the knee. In this instance there was a striking fall of both the whole blood and the plasma chlorides. There was a slight diminution of urine chlorides and a markedly increased output of nitrogen in the urine. Plasma volume and blood counts revealed no evidence of blood concentration. The carbon dioxide combining power remained practically unchanged.

EXTENSIVE BURNS

Observation was made of a group of twelve subjects with extensive burns in whom the lesions were of second or third degree and involved

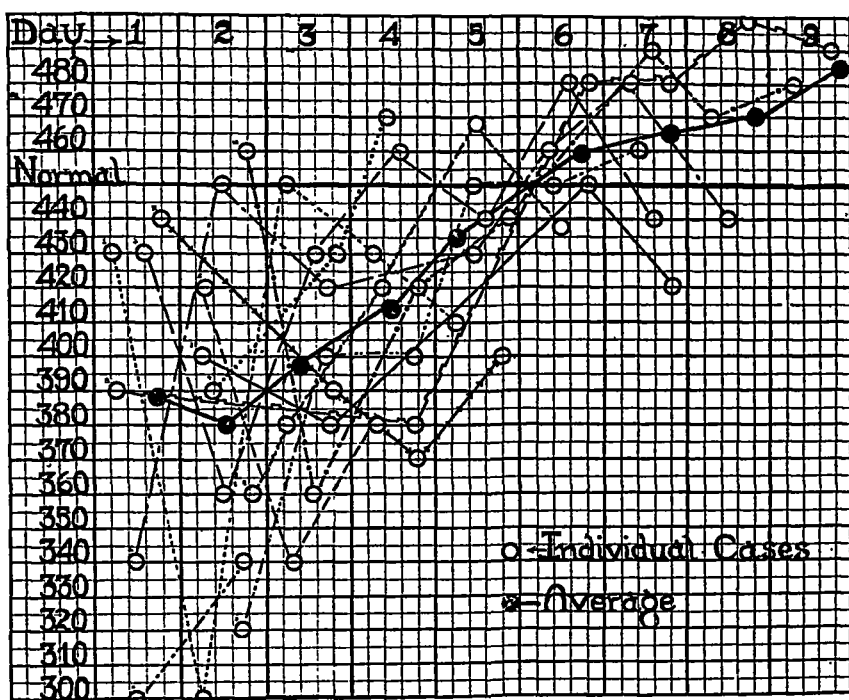


Fig. 1.—Whole blood chlorides following moderate burns.

a cutaneous area varying in size from about 1,000 sq. cm. to a maximum of 24 per cent of the total body surface. Figure 2 shows the whole blood chloride curves of the individual cases as well as the average curve for the group. A fall was noted similar to that seen in less extensive burns. However, this persisted during the entire time that the tissue devitalized by the burn was present. On its separation, elevation to normal limits occurred. It will be observed that the average whole blood chloride curve for the group did not approach normal until after the seventeenth day.

Table 3 summarizes the results in a third degree burn extending from the right ankle to the buttocks. The anterior aspect of the right

TABLE 3.—Blood and Urinary Chlorides in Patient (Case 13) with Third Degree Burn of Right Leg

| Date | Maximum Temperature (Month) | Fluids | | Calories | Diet | Blood | | | | | Hemo- globin, Cent | Red Blood Cells, per Cmm. | Urine | |
|----------|-----------------------------------|----------------|----------------|----------|------|--|--|--|--|--|--------------------------|------------------------------------|--------------------------------|-------------------------------------|
| | | Intake, Cc. | Output, Cc. | | | Carbon Dioxide Capacity, per Cent | Plasma Sodium Chloride, 100 Cc. (Van Slyke), Mg. | Plasma Sodium Chloride, 100 Cc. (Van Slyke), Mg. | Whole Blood Sodium Chloride, 100 Cc. (Van Slyke), Mg. | Whole Blood Sodium Chloride, 100 Cc. (Van Slyke), Mg. | | | Total Nitro- gen, Gm. | Total Sodium Chloride, Gm. |
| 10/17/23 | 100.6 | 3500 | 1850 | 111 | 1.8 | 0.01 | 61.1 | 685 | 456 | 425 | 125 | 6450,000 | 11.21 | 3.91 |
| 10/18/23 | 100.5 | 4150 | 1550 | 84 | 1.8 | 0.01 | 64.8 | 683 | 685 | 425 | 125 | 5400,000 | 8.55 | Trace |
| 10/19/23 | 100.5 | 4000 | 1300 | 75 | 1.8 | 0.01 | 62.3 | 683 | 685 | 425 | 125 | 5400,000 | 11.85 | Trace |
| 10/20/23 | 100.5 | 5150 | 3200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 21.4 | 0.051 |
| 10/21/23 | 100.5 | 7400 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 21.4 | Trace |
| 10/22/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 11.32 | 0.049 |
| 10/23/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 16.42 | Trace |
| 10/24/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 9.44 | Trace |
| 10/25/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 8.0 | Trace |
| 10/26/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.4 | Trace |
| 10/27/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 10.67 | Trace |
| 10/28/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 14.8 | 0.038 |
| 10/29/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 11.20 | 1.55 |
| 10/30/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 8.17 | 5.65 |
| 10/31/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.50 | 6.65 |
| 11/1/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 9.10 | 14.21 |
| 11/2/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.10 | 10.88 |
| 11/3/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 8.57 | 15.33 |
| 11/4/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 10.30 | 2.28 |
| 11/5/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 10.15 | 10.15 |
| 11/6/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.65 | 12.65 |
| 11/7/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/8/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/9/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/10/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/11/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/12/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/13/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/14/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/15/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/16/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/17/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/18/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/19/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/20/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/21/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/22/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/23/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/24/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/25/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/26/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/27/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/28/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/29/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/30/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |
| 11/31/23 | 100.6 | 7000 | 5200 | 68 | 1.8 | 0.01 | 60.0 | 683 | 685 | 425 | 125 | 5400,000 | 12.12 | 12.12 |

thigh revealed a second degree burn. During the early period of observation the diet was inadequate because of the patient's refusal to eat.

The hemoglobin determinations, red blood cell counts and plasma volume observations reveal a striking blood concentration during the first five days, after which blood dilution took place gradually, and a moderate anemia developed. The plasma volume reached a maximum of 64.2 per cent by volume, the red blood cell count fell to 3,010,000 per cubic millimeter, and the hemoglobin dropped to 69 per cent.

The whole blood and plasma chlorides showed a gradual fall during the first nine days and then returned slowly to normal. During this time there was no true relationship between the plasma volume and the

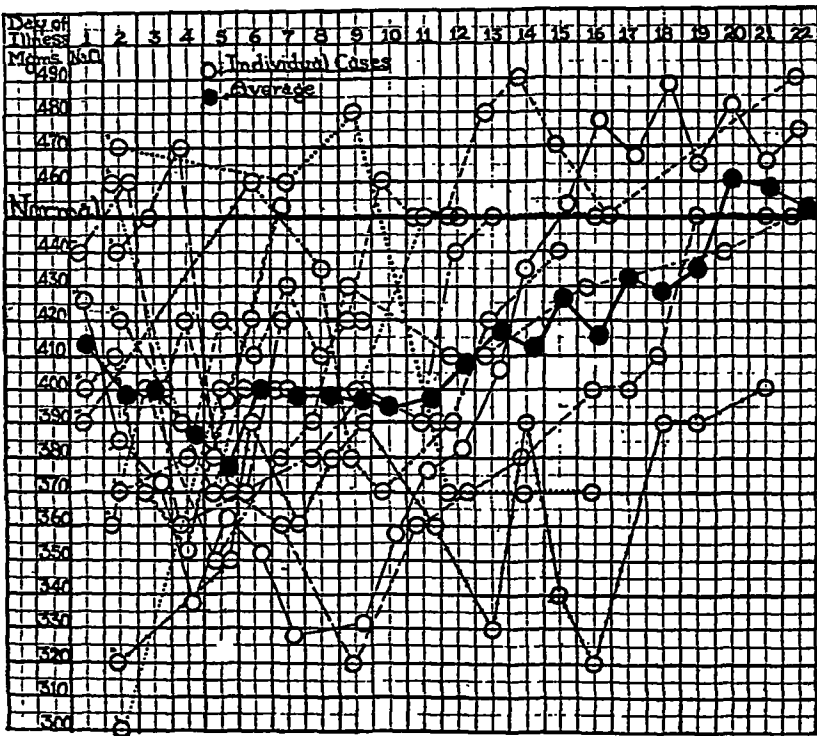


Fig. 2.—Whole blood chlorides following extensive burns.

chloride values (figs. 3 and 4). During the first two days, when the blood was most concentrated as evidenced by the low plasma volume, the plasma and whole blood chlorides were just beginning to fall and did not reach the low point until the tenth day when the plasma volume had returned to normal. The urinary chlorides were strikingly diminished and this diminution is seen to bear a direct relationship to the lowered plasma chlorides (fig. 5). In convalescence, when most of the sloughs had separated, there was a sudden outpouring of chlorides in the urine (fig. 6) quite similar to that seen following the crisis in pneumonia. After this time there was a fairly normal ratio between the salt intake and the chloride output.

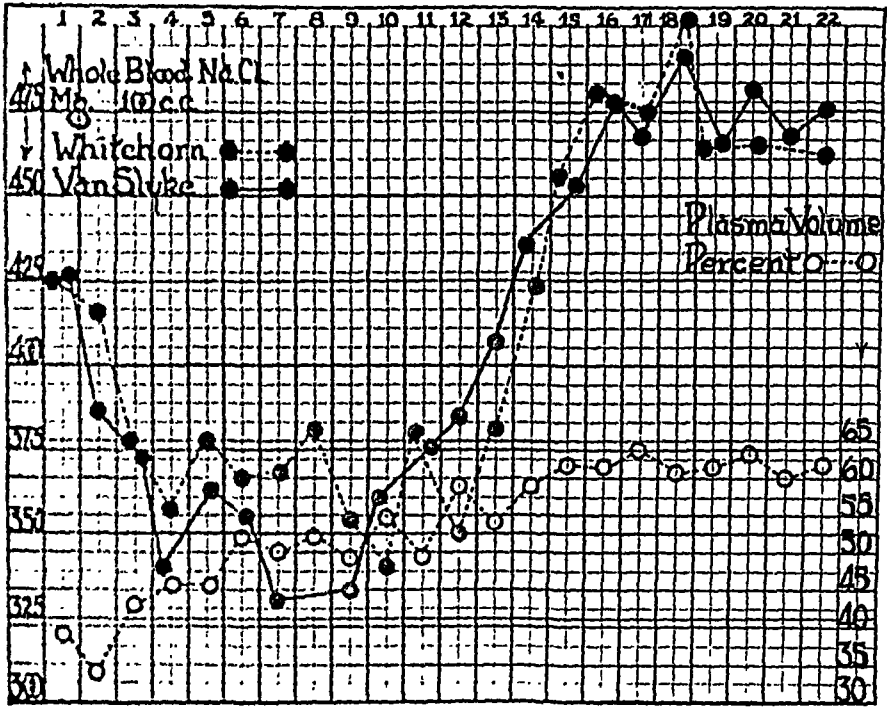


Fig. 3 (case 13).—Whole blood chlorides in relation to plasma percentage by volume.

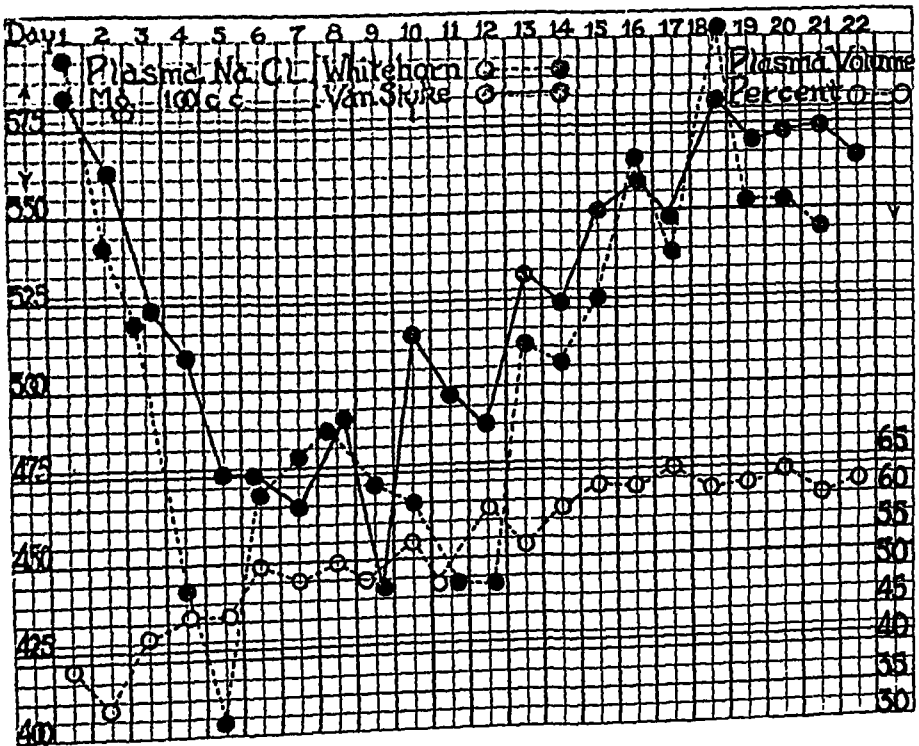


Fig. 4 (case 13).—Plasma chlorides in relation to plasma percentage by volume.

The nonprotein nitrogen of the blood was relatively high during the first ten days of observation and the nitrogen output in the urine was tremendously increased (fig. 6), so that the patient was in negative balance until practically all the sloughs had separated.

During the entire period of observation there was no characteristic alteration in the carbon dioxide combining power of the plasma. In spite of the marked metabolic disturbance the temperature elevation was not high.

In table 4 are summarized the results of whole blood chloride and nonprotein nitrogen determinations in relation to red blood cell counts

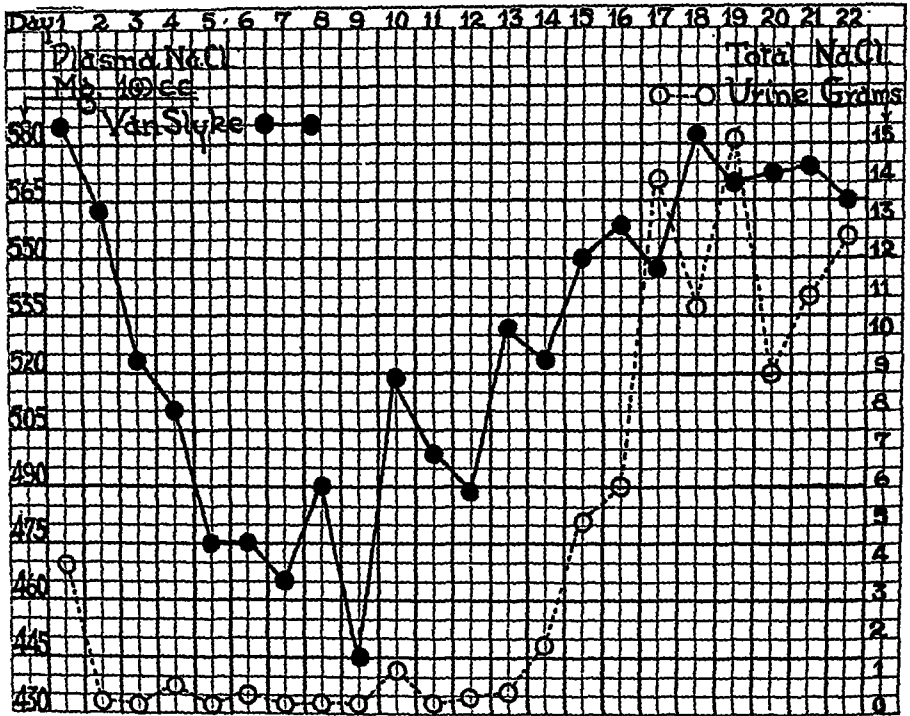


Fig. 5 (case 13).—Plasma and urinary chlorides during period of three weeks following burn.

and hemoglobin contents. In this group of cases there has been observed a definite lowering of the whole blood chlorides. Alterations of the hemoglobin and red cell count have not paralleled the changes in the whole blood chlorides. In a number of instances low whole blood chlorides were observed when the red blood cell count and hemoglobin percentage were normal or below.

Figure 7 shows the relationship of whole blood chlorides to temperature and pulse in a person who had a second degree burn of the abdomen, legs and hands which involved altogether about 18 per cent of the total body surface. It is seen that the low blood chlorides persisted after the temperature had reached normal.

TABLE 4.—*Blood Chlorides and Nonprotein Nitrogen in Relation to the Hemoglobin Percentage and Red Blood Cell Counts*

| Case | Date | Whole Blood Sodium Chloride per 100 Cc., Mg. | Nonprotein Nitrogen per 100 Cc., Mg. | Red Blood Cells, per Cmm. | Hemoglobin, per Cent |
|---------|----------|--|---|---------------------------------|-------------------------|
| 2..... | 1/29/25 | 420 | 37.0 | | ... |
| | 1/30/25 | 340 | 45.0 | 5,000,000 | 96 |
| 3..... | 1/29/25 | 300 | 25.3 | | ... |
| | 1/30/25 | 340 | 20.0 | 4,520,000 | 94 |
| 4..... | 1/21/25 | 500 | 31.6 | 4,200,000 | 80 |
| | 1/22/25 | 400 | 31.9 | 4,370,000 | 81 |
| | 1/23/25 | 450 | 33.0 | 4,510,000 | 90 |
| 5..... | 8/18/25 | 360 | 33.3 | 4,250,000 | 86 |
| | 8/19/25 | 379 | 37.0 | 4,270,000 | 87 |
| | 8/20/25 | 421 | 40.0 | 4,020,000 | 78 |
| | 8/21/25 | 478 | 26.0 | 3,650,000 | 78 |
| 6..... | 8/15/25 | 460 | 30.9 | 4,260,000 | 78 |
| | 8/16/25 | 430 | 31.2 | | ... |
| | 8/17/25 | 390 | 25.9 | 3,520,000 | 82 |
| | 8/18/25 | 370 | 28.5 | 3,590,000 | 75 |
| | 8/19/25 | 400 | 28.0 | 3,920,000 | 80 |
| 7..... | 7/29/25 | 460 | 28.2 | | ... |
| | 7/30/25 | 360 | 30.0 | 3,990,000 | 82 |
| | 7/31/25 | 420 | 30.0 | 4,240,000 | 83 |
| | 8/ 1/25 | 440 | 33.0 | 3,920,000 | 80 |
| | 8/ 3/25 | 490 | 26.1 | 4,000,000 | 85 |
| 8..... | 1/21/25 | 440 | 32.3 | 4,530,000 | 90 |
| | 1/22/25 | 460 | 30.9 | 4,490,000 | 88 |
| | 1/24/25 | 360 | 31.2 | 4,620,000 | 90 |
| | 1/28/25 | 380 | 34.1 | 4,320,000 | 80 |
| 9..... | 3/11/25 | 300 | 39.5 | 4,820,000 | 83 |
| | 3/12/25 | 430 | 46.0 | | ... |
| | 3/13/25 | ... | 26.1 | 4,580,000 | 90 |
| 10..... | 11/10/24 | ... | 38.0 | 4,650,000 | 90 |
| | 11/11/24 | 370 | 40.6 | 4,000,000 | 93 |
| | 11/13/24 | 380 | 34.1 | | ... |
| | 11/14/24 | 420 | | 3,590,000 | 74 |
| | 11/18/24 | 420 | 33.0 | 3,750,000 | 72 |
| 11..... | 8/22/25 | 320 | 25.9 | | ... |
| | 8/25/25 | 350 | 25.0 | 3,840,000 | 77 |
| | 8/26/25 | 390 | 30.0 | 4,540,000 | 72 |
| | 8/28/25 | 380 | 32.3 | 3,540,000 | 73 |
| | 8/29/25 | 390 | 26.1 | 3,790,000 | 68 |
| | 9/ 2/25 | 330 | 26.8 | 3,680,000 | 70 |
| | 9/11/25 | 400 | 24.2 | 3,050,000 | 60 |
| | 9/17/25 | 450 | 27.5 | 3,750,000 | 67 |
| | 7/28/25 | 400 | 33.0 | 4,720,000 | 105 |
| 12..... | 7/29/25 | 410 | 28.9 | 4,890,000 | 98 |
| | 7/30/25 | 370 | 27.0 | 4,340,000 | ... |
| | 7/31/25 | 354 | 30.5 | 4,220,000 | 93 |
| | 8/ 1/25 | 396 | 33.5 | 4,420,000 | 90 |
| | 8/ 2/25 | 421 | 40.0 | 4,360,000 | 84 |
| | 8/ 9/25 | 454 | 40.0 | 4,480,000 | 90 |
| | 10/20/25 | 426 | 36.8 | | ... |
| | 10/21/25 | 385 | 48.2 | | ... |
| 13..... | 10/22/25 | 374 | 60.8 | 6,450,000 | 123 |
| | 10/23/25 | 338 | 44.4 | 5,440,000 | 111 |
| | 10/24/25 | 362 | 53.8 | 5,400,000 | 106 |
| | 10/25/25 | 352 | 51.2 | 4,600,000 | 100 |
| | 10/26/25 | 329 | 55.0 | 5,400,000 | 93 |
| | 10/27/25 | ... | 40.0 | 4,500,000 | 78 |
| | 10/29/25 | 358 | 43.2 | | 78 |
| | 10/30/25 | 376 | 50.0 | 4,600,000 | ... |
| | 11/ 4/25 | 454 | 25.9 | 3,550,000 | 76 |
| | 11/ 5/25 | 478 | 31.0 | 3,530,000 | 72 |

COMMENT

The observations here reported reveal a striking alteration of chloride metabolism in cutaneous burns. To explain this phenomenon, diet, body temperature, loss of chlorides through vomiting, alkali therapy, altered renal threshold, concentration of blood, and finally transudation of plasma at the site of the burn must be considered.

Mayer¹² reduced the sodium chloride of his diet to 1.25 Gm. per day and after weeks of observation did not notice any deleterious effect. Austin and Jonas¹³ concluded from a series of feeding experiments in dogs that the plasma chlorides could not be elevated or lowered by alterations in chloride intake except in a very transient manner. Underhill and Wakeman¹⁴ found that the concentration of chlorides in the blood remains practically constant during fasting. In the cases presented, approximately from 7 to 9 Gm. of sodium chloride was given daily. Nevertheless, marked changes were found in the blood chlorides. In case 13 there was a low chloride intake during the early period of observation due to the patient's refusing to take his diet. This would in part account for the practical absence of sodium chloride in the urine during this period. However, even after he began to ingest sodium chloride an appreciable amount did not appear for a number of days. When the devitalized tissue at the site of the burn separated, there was an outpouring of sodium chloride in the urine which was greater than that provided by the diet (table 3 and fig. 6). These facts suggest that storage of sodium chloride takes place.

The exact importance of fever in relation to chloride metabolism is not clear, as pointed out by Peabody.¹⁵ McLean¹⁶ found that in fever the average renal threshold for chlorides was 542 mg. per hundred cubic centimeters of plasma instead of the normal value, 562 mg. Practically all patients with extensive burns are febrile during convalescence. However, in this series one patient (case 14) revealed a persistently low whole blood chloride after the temperature had become normal (fig. 7).

12. Mayer, A.: Observations sur l'urine de l'homme sain soumis à une alimentation pauvre en chlorure de sodium, *Compt. rend. Soc. de biol.* **58**:377, 1905.

13. Austin, J. H., and Jonas, L.: Effect of Diet on the Plasma Chlorides and Chloride Excretion in Dogs, *J. Biol. Chem.* **33**:91-101 (Jan.) 1918.

14. Underhill, F. P., and Wakeman, E. T.: The Behavior of Chlorides Introduced into the Blood Under Normal and Nephritic Conditions, *J. Biol. Chem.* **54**: 701-715 (Dec.) 1922.

15. Peabody, F. W.: Studies of the Inorganic Metabolism in Pneumonia with Especial Reference to Calcium and Magnesium, *J. Exper. Med.* **17**:71-82, 1913.

16. McLean, F. C.: The Numerical Laws Governing the Rate of Excretion of Urea and Chlorides in Man, II, The Influence of Pathological Conditions and Drugs on Excretion, *J. Exper. Med.* **22**:366-388, 1915.

It should further be noted that in case 13 (table 3) the whole blood and plasma chlorides, after falling to a low level, returned to normal limits while the temperature was still elevated. Accordingly, temperature per se could not explain this metabolic disturbance.

Lowering of the blood chlorides is observed when the normal passage of hydrochloric acid from the stomach to the intestines is interrupted. This loss of chlorides has been assumed by some to explain the low blood chlorides observed in pyloric stenosis,¹⁷ pernicious vomiting of pregnancy,¹⁸ and intestinal obstruction. Haden and Orr,¹⁹ however, have

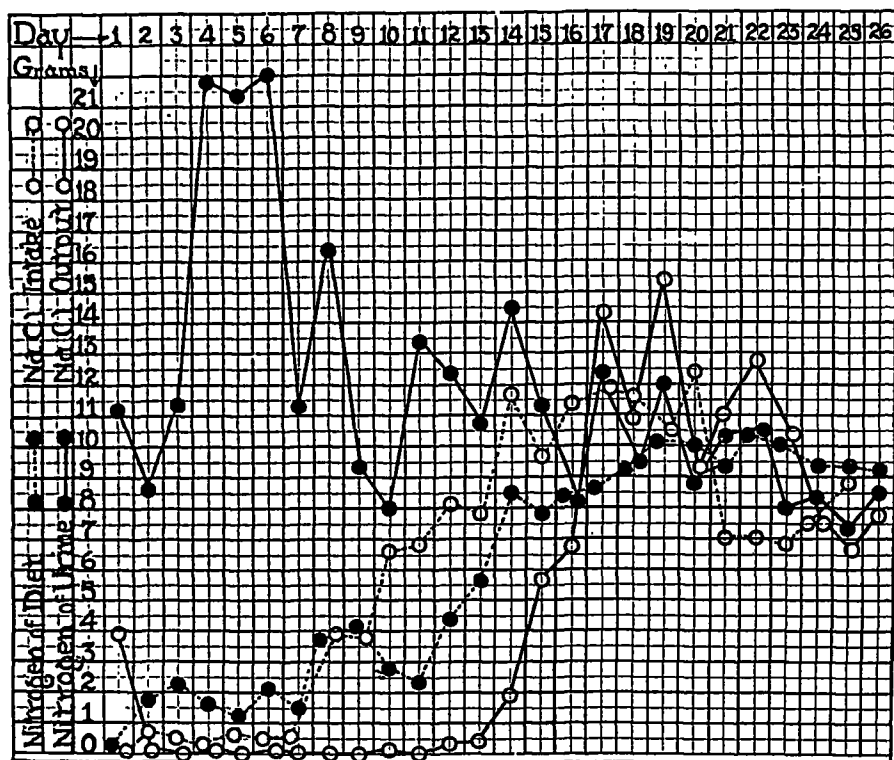


Fig. 6 (case 13).—Nitrogen and sodium chloride of diet and urine.

shown that the same fall in blood chlorides occurs in rabbits with intestinal obstruction although rabbits cannot vomit. They have further shown by analysis of the vomitus²⁰ that the chloride content is not suffi-

17. MacCallum, W. G.; Lintz, J.; Vermilye, H. N.; Liggett, T. H., and Boas, E.: The Effect of Pyloric Obstruction in Relation to Gastric Tetany, *Bull. Johns Hopkins Hosp.* **31**:1-7 (Jan.) 1920. Murray, H. A.: The Chemical Pathology of Pyloric Occlusion in Relation to Tetany, *Arch. Surg.* **7**:166-196 (July) 1923.

18. De Wesselow, O. L. V.: The Variations in the Chloride Content of the Blood, *Internat. Clin.* **3**:191-199, 1924.

19. Haden, R. L., and Orr, T. G.: Chemical Changes in the Blood of the Dog After Intestinal Obstruction, *J. Exper. Med.* **37**:365-375 (March) 1923.

20. Haden, R. L., and Orr, T. G.: Chemical Changes in the Blood of the Dog After Pyloric Obstruction, *J. Exper. Med.* **37**:377-381 (March) 1923.

cient to make up the deficiency observed in the blood. In this group of cases, vomiting was not a contributing factor to the lowering of the blood chlorides for in only one case did this occur and then on two occasions only.

Von Noorden²¹ has mentioned the possibility of depleting the body of sodium chloride by the administration of large quantities of alkaline carbonates. This may explain the observation of Haden and Orr²² that dogs with intestinal obstruction were in worse physical condition when given sodium bicarbonate than untreated animals were. Alkalis were not administered in any of the cases under discussion and so could not

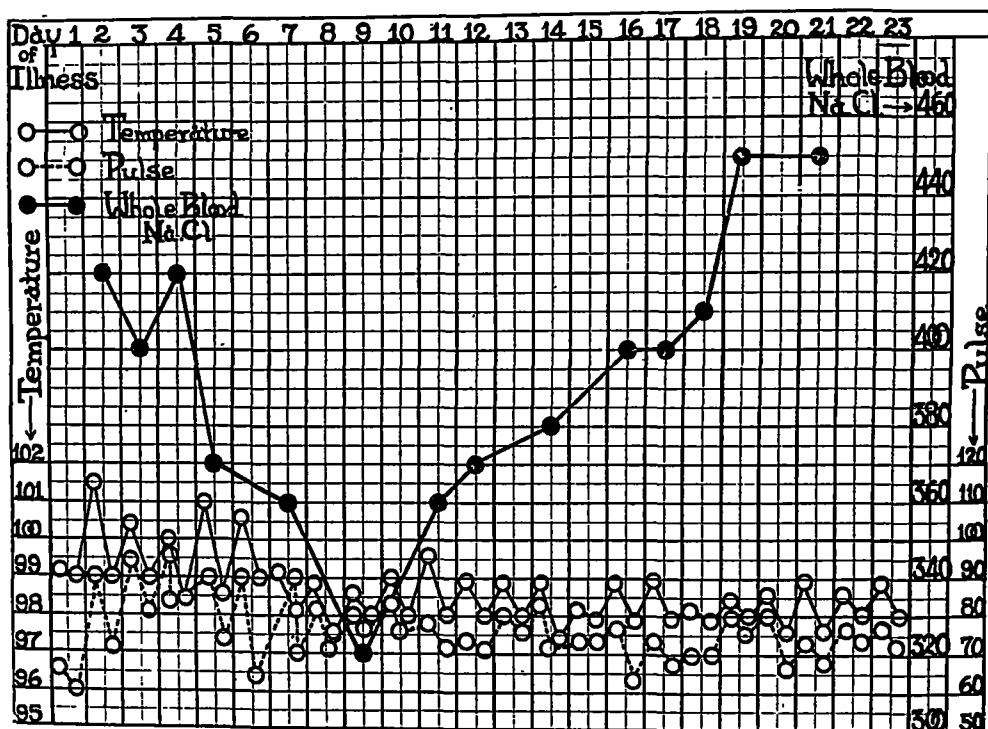


Fig. 7 (case 14).—Whole blood chlorides in relation to temperature and pulse.

possibly be a contributing factor. In those cases in which the carbon dioxide combining power of the plasma was determined, there was no striking elevation at the time the blood chlorides were at a low level.

Another possible explanation of the low whole blood and plasma chlorides is a lowering of the renal threshold with resulting blood depletion. In McLean's¹⁶ exhaustive investigation of this problem he found that the threshold in diabetes mellitus averaged 512 mg. per hundred

21. Von Noorden, C.: *Metabolism and Practical Medicine*, London, William Heinemann, 1907, 1:418.

22. Haden, R. L., and Orr, T. G.: The Effect of Sodium Chloride on the Chemical Changes in the Blood of the Dog After Pyloric and Intestinal Obstruction, *J. Exper. Med.* 38:55-71 (July) 1923.

cubic centimeters of plasma instead of the value 562 mg. found in normal individuals. He further observed that certain diuretics caused a lower threshold, which resulted in chloride depletion of the plasma to a point lower than the lowest value seen in normal persons. Were this the cause of the low whole blood and plasma chlorides in burned patients, examination of the urine would show an increased chloride output. In case 13 there was practically a complete suppression of urinary chlorides (table 3 and fig. 5). Therefore, alteration of the renal threshold would not explain the low blood chlorides observed. The diminished output of chlorides in the urine appears quite analogous to that observed in pneumonia¹⁰ and is not primarily renal. When the plasma chlorides fall below the renal threshold excretion ceases. As the blood chlorides again rise above the renal threshold, excretion begins.

The low values of the whole blood and plasma chlorides might also be attributed to blood concentration. The sodium chloride content of normal plasma varies from 560 to 640 mg. per hundred cubic centimeters, while that of the corpuscles is about 310 mg.²³ Any factor that alters the proportion of cells to plasma in circulating blood changes the value of the whole blood chlorides. It may be seen in the determinations presented (fig. 3) that the whole blood chlorides remained low even after the plasma volume had returned to normal limits, and the red blood cell count and hemoglobin revealed no concentration. Were the low chloride values of whole blood due to a simple process of concentration, no alteration in the plasma chlorides would be anticipated. However, in those cases in which plasma chlorides were determined, the depression of the chlorides (fig. 4) was as striking as that observed in whole blood.

It might also be urged that the fall in blood chlorides may be due to the loss of sodium chloride at the site of the burn during the development of edema. The blood depletion would continue until tissue chlorides were mobilized. This might seemingly explain the initial fall which is occasionally seen in extensive burns, but were this the true explanation, the normal balance would be reestablished in a few hours. In case 1 (table 1) the intensity of the thermal agent was sufficient to cause a marked edema but it caused little tissue destruction. Were the lowering of blood chlorides due to simple edema, a fall would be anticipated in this instance; however, no change occurred. Were this the explanation of the phenomenon observed, the lowering of the blood chlorides would be transient, but from the other cases investigated it seems that the low values persist as long as sloughs are present.

Finally, it might be asserted that the persistent low blood and plasma chlorides are due to loss of chloride and plasma in the wound. Undoubt-

23. Norgaard, A., and Gram, H. C.: Relation Between the Chloride Content of the Blood and Its Volume Per Cent of Cells, *J. Biol. Chem.* **49**:263-278 (Dec.) 1921.

edly some loss takes place by this route, but it does not entirely explain the picture. In case 13, in which the burn was practically all third degree, the blood chlorides remained at such a low level that there was almost a complete suppression of urinary chlorides. When all the sloughs separated, leaving a raw granulating wound (fig. 8) much more favorable for the loss of plasma, the blood chlorides, instead of remaining at a low level as would be anticipated, immediately rose. There was a parallel rise of the urinary chlorides and later an outpouring of chlorides (fig. 6), which was greater than the daily intake. Finally, a fairly normal ratio between the sodium chloride intake and output would not become established until healing was complete if this explanation were correct.

The chloride metabolism in burns is a complex mechanism, undoubtedly involving a number of factors. These have been enumerated and

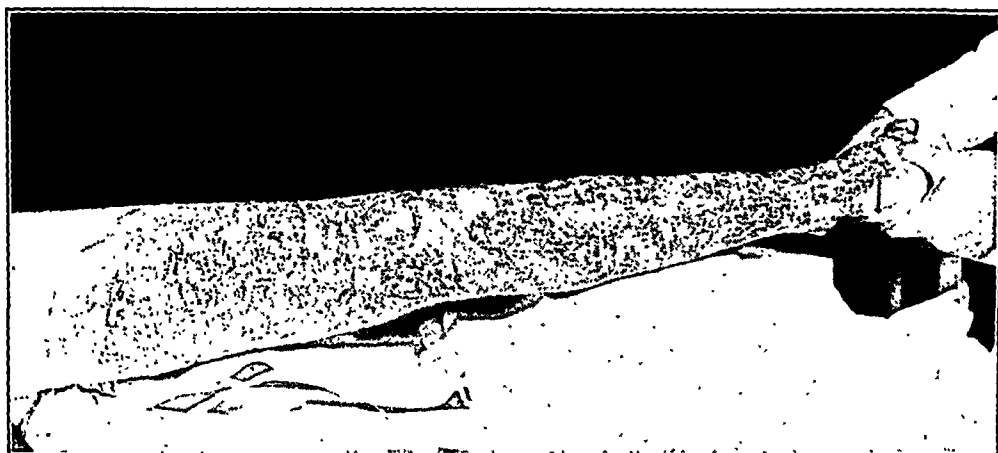


Fig. 8 (case 13).—Granulating wound on twenty-fourth day.

no one of them alone explains satisfactorily the alterations noted. There probably is some direct loss of sodium chloride from the lesion, but this does not appear to be great, because the blood chlorides reach normal and chloride excretion in the urine begins as soon as the sloughs separate, although a granulating wound still remains.

In lobar pneumonia there is sodium chloride retention that is not accounted for by analysis of the involved lung tissue.¹⁵ The chloride seems rather to be concealed in combination with all the tissues and at the crisis there is a sudden outpouring of chlorides. A quite similar elevation of blood chlorides and the appearance of large quantities of sodium chloride in the urine took place in the case detailed in table 3 as soon as the sloughs separated. This observation suggests that sodium chloride had been stored in the tissues.

The clinical condition of the patients under discussion has been reflected better by the level of the blood chlorides than by observations of

the nonprotein nitrogen. The analogy between intestinal obstruction, which is thought to be an intoxication due to some protein derivative, and the toxemia of burns is a close one. The clinical picture, the finding of increased protein catabolism, and alterations in the chloride metabolism are strikingly similar. Haden and Orr²² have presented the conception that in intestinal obstruction sodium chloride combines with the primary toxic material before it has an opportunity to cause tissue protein destruction. In a series of admirable studies they have demonstrated the protective and detoxifying effect of sodium chloride in intestinal obstruction. From the present observations and the analogy with intestinal obstruction it would seem that a rational therapy in burns would consist of the judicious administration of sodium chloride in an attempt to correct the metabolic deficiency.

SUMMARY AND CONCLUSIONS

In observations on the chloride metabolism of thirty-one burned patients, the lowering of the whole blood and plasma chlorides was significant.

The fall in the blood chlorides was not wholly explained by alteration of the renal threshold, diet, fever, exudation, blood concentration, nor by vomiting.

There was suggestive evidence that retention of sodium chloride took place.

The diminished sodium chloride output in the urine was not due to primary kidney change but rather to a lowering of the plasma chlorides to a level below the renal threshold.

The disturbance of chloride metabolism seemed proportionate to the amount of tissue devitalized.

The retained chloride was not present in the blood in some undetermined form.

There was evidence of an increased protein catabolism.

The observations suggest the administration of sodium chloride to correct the deficiency.

CORRECTION

Dr. Albert J. Scholl, Los Angeles, reports an error in the Review of Urologic Surgery appearing in the April issue of the *ARCHIVES OF SURGERY*. In the editorial note on page 937, the statement to the effect that Dr. Hager of the University of Wisconsin has had an extensive experience in the treatment of schistosomiasis in Santo Domingo should read:

"Hager of the University of Wisconsin has had considerable experience in the treatment of tropical diseases indigenous to the West Indies."

A REVIEW OF UROLOGIC SURGERY

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(Continued from page 152)

BLADDER

Diverticulum.—Gayet and Cibert³⁷ reviewed their cases of diverticulum of the bladder. They state that they are inclined to modify their previous opinion that congenital diverticula were far more frequent than acquired diverticula. In twenty-two cases they found only five in which the disease was probably congenital. In the other seventeen there was an obstacle to the flow of urine; in ten cases the obstacle was prostatic adenoma, in six it was a stricture and in one a suppurative cyst of the prostate. All patients were males. One case was interesting to study from an etiologic standpoint; there was no kidney, no ureter, no seminal vesicle or vas deferens on the left side. Instead there were two large diverticular pouches on the left side of the bladder. Stiles reported a somewhat similar case. The authors state, "Certain diverticula, of rather rare occurrence, are due to incomplete development of ureteral buds, or seminal buds." They also mention the following hypothesis, which had been first stated by Paul Delbet: Congenital diverticula may have their point of origin in the nondevelopment of a double ureter. Gayet and Cibert do not wish to insist on these hypotheses, because of the still unsettled state of knowledge of the embryology of the bladder; they state that an area particularly favorable to the development of diverticula exists in the region of the ureteral meatus which may in certain cases be included in the malformation, appear on the edges of the diverticular orifice or even be situated in the diverticulum itself. Noninfected, nonadherent diverticula are rare; most often there is some peridiverticulitis. Often the

37. Gayet, G., and Cibert, J.: Quelques cas de diverticules de la vessie, J. d'urol. méd. et chir. 19:473-505, 1925.

ureter pressed by the pocket is dilated above and the corresponding kidney is dilated and septic. In fifteen cases of Gayet and Cibert death occurred in six cases in which operation was not performed and in three of nine cases in which operation was performed. In the former cases the diverticula, pyuria and fistulas rendered the prognosis serious, whereas in the latter either the disease was definitely cured or, at least, the more severe symptoms were relieved. The authors agree on the necessity of a radical operation and particularly on the great importance of early diagnosis.

Mercier³⁸ states that interrupted micturition is not characteristic of diverticulum of the bladder alone; it may occur even in a moderate interureteral bar. Its mechanism is not the same as in the cases of diverticulum. The mechanism when a bar is present is somewhat similar to that observed in the watergate mechanism. During the first micturition, under the influence of contraction of the detrusor, progressively prominent and shuts off under the influence of the interureteral bar from which urine cannot flow. At rest, the ureter dilates a little and urine then escapes towards the vesical neck. A second micturition will evacuate the fluid which has passed in front of the bar. The mechanism depends on a number of factors. The bar must be sufficiently developed and vesical contraction must be strong. When the interureteral bar is moderately prominent, it allows a sufficient amount of back of it a certain quantity of urine during micturition. In extreme cases marked hypertrophy of the prostate gland causes a definite and slightly contractile depression, causing a permanent retention of residual urine.

Ward,³⁹ in considering vesical diverticula, remarks that they may be entirely congenital in origin, but that more often they are the result of a dilatation of the vesical neck, which causes a large enough neck to produce symptoms. In one of Ward's cases, that of a boy aged 15 years, there was a diverticulum and many fistulas. The commonest symptoms result from infection of adjacent areas in the prostate. It is not surprising that inflammation extends even into the rectum. In this form, for, although the wall of the diverticulum is thin, the detrusor muscle is always intact and is independent of that of the bladder itself. The ring of muscle which is often seen around the orifice, has only some of the function of a sphincter and does not, in a very imperfect degree. Therefore, when the patient micturates, the bladder empties itself in part through the diverticulum and through the urinary meatus into the urethra and through the penile urethra.

38. Mercier, O.: De la micturition interrompue par la barre interuretrale. *Bull. d'Urol. med. et chir.* 20:97-102, 1925.

39. Ward, R. O.: A Clinical Study of Benign Prostatic Hypertrophy. *Brit. J. Surg.* 13:144-157 (July) 1925.

orifice into the diverticulum. When the bladder is empty the diverticulum sometimes discharges its contents, but usually the act is very incompletely performed, and probably, in every case, some urine remains in it, even if special postures are adopted to encourage drainage by gravity, and, indeed, even after catheterization.

The cystoscope and cystogram provide accurate means of diagnosis. Palliative measures are unsatisfactory and excision is the only satisfactory means of cure. Results of such operations are good but care must be taken that coexistent obstruction is not overlooked. When obstruction is present it must be suitably dealt with.

[ED. NOTE.—It is very important that the accompanying obstruction of the bladder be dealt with properly. Some urologic surgeons state that if the obstruction is removed the diverticulum need not be disturbed. This is a somewhat radical view but it unquestionably holds true in the cases of small uninfected pouches. Removal of the obstruction, whether by means of a prostatectomy or by excision of the vesical neck, increases the operative risk only slightly. In a series of fifty recently reported cases in which the diverticulum alone was excised, three (6 per cent) patients died. In a second series of thirty-seven cases in which excision of the diverticulum and prostatectomy were performed, three (8.1 per cent) patients died.

At times the suprapubic vesical wound is slow to heal after an operation for the removal of a diverticulum. While this may be due to the presence of an obstruction at the neck of the bladder, the latter may sometimes be impossible to demonstrate, and we have been inclined to feel that the poor contractility of the wall of the bladder and the vesical deformity might be responsible for the persistent suprapubic urinary sinus.]

Jarosz⁴⁰ reports a series of cases of diverticulum of the bladder from Hildebrand's Clinic in Berlin. Pagenstecher states that congenital diverticula develop on the basis of a second bladder anlage. The musculature of the bladder withstands the pressure of urine for a time but later gives way to the formation of a sac or diverticulum. The diverticula are prone to develop first in the region of the ureteral outlets, next in the anterior or posterior wall, on the side walls, and last in the dome of the bladder. Blum states that congenital diverticula develop either through a defect in the formation of the bladder, an anomaly in the fetal anlage or as a result of urinary retention in fetal life. The developing type of diverticulum forms in later life as a result of straining on urination and an increase in the intravesical pressure. The condition may result from stone, prostatic hypertrophy,

40. Jarosz, H.: Zur Kenntnis der Harnblasendivertikel, *Ztschr. f. Urol.* 19: 722-733, 1925.

urethral stricture or even from phimosis. Zacharisson found a case in a boy, aged 21 months, which was caused by a marked phimosis. Spinal diseases may also cause urinary retention, muscular spasm and the formation of a sac. Diverticula may also be associated with hernia. Englisch reported ten single and six bilateral diverticula found in hernial sacs. There is an increasing number of cases being diagnosed since the perfection of diagnostic methods. In 1901 Durrieux found 194 cases in an extensive review of the literature. Cholzoff in 1911 reported seventy cases of congenital diverticulum and Englisch reported 250 cases of stone forming in diverticula. Jarosz reports nine cases. In two cases in which operation was performed, one for removal of the diverticulum and prostatectomy and the second for removal of a stone from the diverticulum, death ensued. In a third case, in which the diverticulum was in a hernial sac, operation was performed successfully. In the remaining cases surgical treatment was not instituted. In one there were multiple diverticula, in another the diverticulum was complicated by carcinoma.

[Ed. Note.—These cases were observed during a period of fifteen years. During the same period 181 cases of prostatic hypertrophy, twenty-four of vesical stone, sixty-one of vesical tumor and thirty of other surgical diseases of the bladder were observed. There was a small number of cases in which operation was performed and most of these occurred from ten to fifteen years ago; the results obtained were in accordance with the results for similar operations of that period. Since that time there have been remarkable advances in the diagnosis and surgical approach in cases of lesions of the bladder. In the earlier cases in which operation was performed the condition was often discovered accidentally, and the operation was carried out without consideration of the complicating lesion and, at times, of the presence of marked infection. The mortality was high and the operative results were only fair. Recent methods of urologic diagnosis, however, make it possible to recognize the disease, the associated lesion and the infection, and to suggest the type of surgical procedure that will produce the most satisfactory results in a given case. A review of the theories of the formation of diverticulum is given.

Vesical diverticula are probably due, as Jarosz states, primarily to embryologic defects in the bladder, either a weakening of the musculature, usually at the base of the bladder, or a definite hiatus in the wall of the bladder. Targett asserts that they are due to an interruption of the muscle fibers in the base of the bladder by the entrance of the large vesical arteries in this region. The actual distention and dilatation of the sac probably result in most cases from obstruction to the outlet of the bladder. Diverticula are often seen in young children and occasionally in the fetus. In a 5 months embryo, seen at the Mayo Clinic,

two definite diverticula were found, one in the region of each ureteral orifice. The one near the right orifice was composed of all the coats of the bladder and was 1 cm. in depth. Kelly states:

Diverticula of the bladder are usually formed from small preexisting pouches or hernias in the bladder which become enlarged by pressure and later come into prominence through stagnation of urine and inflammation.

According to Hinman, diverticula result from anatomic, pathologic and mechanical factors, and in this sense the condition is acquired. He states:

A mild chronic urinary obstruction in association with the necessary anatomic or pathologic predisposing condition of the bladder wall is particularly conducive for the development of diverticula.

The mortality, both without and with operation, up to recent years has been high. Englisch, in 1894, found that in 83.1 per cent of the reported cases of vesical diverticula the patients had died as a result of the abnormality. At this time few operations were performed on the bladder, and in most cases the diverticula were probably seen only in the late stages. In 1910 Fischer collected records of forty-eight cases in which, with and without operation, thirty-two patients (66.7 per cent) died. Of twenty-eight patients subjected to operation, eight (40 per cent) died. In 1922, Kneise and Schulze compiled records of thirty-five cases from the German literature and added eighteen of their own, in which radical operations had been performed. Four patients (7.7 per cent of fifty-two) died following operation.]

Bladder Tumors.—MacKenzie⁴¹ reports 288 cases of vesical neoplasms from the Royal Victoria Hospital. Table 2 gives the method of treatment and the results obtained.

MacKenzie liberates the bladder by extraperitoneal resection which permits drawing the bladder forward and out of the abdomen. The peritoneal fold is carefully separated through a suprapubic incision in the median line, the urachus is liberated, clamped, cut, and the upper stump ligated. Traction is then applied to the lower stump to facilitate the separation of the peritoneum from the posterior wall of the bladder. If the case is one of benign papilloma, complete destruction with cautery well into the wall of the bladder is sufficient, the cauterization extending through the wall of the bladder. If the condition is malignant the underlying wall of the bladder is widely excised. If the ureteral orifice is involved the ureter is transplanted. When radium was used emanation seeds were employed and inserted through a hollow needle. When deep roentgenologic treatments were given, they consisted of a series

41. MacKenzie, D. W.: *Bladder Neoplasms*, Surg. Gynec. Obst. **41**:773-778 (Dec.) 1925.

TABLE 2.—Treatment and Results in Two Hundred and Eighty-Eight Cases of Vesical Neoplasm (MacKenzie)

| | Cases | Total |
|--|-------|-------|
| Papilloma of bladder, malignant..... | 39 | |
| Repeated fulguration: | — | |
| Cured | 12 | |
| Improved | 7 | 19 |
| Cystotomy and cauterization: | | |
| Cured | 5 | |
| Improved | 1 | 6 |
| Excision: | | |
| Cured | 4 | |
| Improved | 2 | 6 |
| Treatment by cautery and radium: | | |
| Cured | 4 | |
| Improved | 1 | 5 |
| No treatment | 3 | 3 |
| Carcinoma | 78 | |
| Inoperable, no treatment..... | 27 | 27 |
| Excision: | | |
| Cured | 7 | |
| Recurrence | 6 | |
| Died | 1 | 14 |
| Excision and cauterization: | | |
| Cured | 2 | |
| Improved | 1 | 3 |
| Excision and treatment with radium: | | |
| Cured | 2 | |
| Improved | 2 | 4 |
| Treatment by cautery and radium: | | |
| Cured | 4 | |
| Recurrence | 1 | |
| Died | 1 | 6 |
| Excision and transplantation of ureter: | | |
| Cured | 1 | 1 |
| Excision and transplantation of ureter and treatment with radium: | | |
| Died (this patient died from metastasis five months later) | 1 | 1 |
| Cauterization and fulguration being only palliative efforts in advanced cases: | | |
| Cured | 1 | |
| Recurrence | 4 | |
| Not improved | 5 | |
| Died | 1 | |
| Deep roentgen-ray, inoperable cases: | | |
| Improved | 2 | |
| Not improved | 3 | |
| Died | 1 | 6 |
| Suprapubic drainage for advanced inoperable conditions: | | |
| Not improved | 1 | |
| Died | 4 | 5 |

of four treatments of 200 kilovolts, 5 milliamperes, distance 40 cm. and exposure sixty minutes. The rays were filtered through 1 mm. of copper and 1 mm. of aluminum. One exposure was given over the symphysis, one over the sacrum, and one over the right and left sacroiliac joints. This was repeated at the end of six weeks.

Fullerton⁴² draws attention to the confusion that exists at present in classifying epithelial tumors into benign and malignant groups and recommends Broders' classification, which depends on the proportion of differentiated to nondifferentiated cells in the section. The differentiated cells resemble those of the epithelial lining of the normal bladder. The undifferentiated cells are the spherical and irregular cells, with prominent nucleoli. Four grades are recognized, the first being one-fourth undifferentiated, the second one-half, the third three-fourths, and the fourth entirely composed of undifferentiated cells.

Fullerton further calls attention to the large proportion of late diagnoses that occur on account of the negligent way in which these patients are treated without investigation for years. Vesical symptoms, and especially hematuria in late adult life, are too serious to be trifled with and demand the most prompt and careful urologic investigation.

All tumors of the bladder are more common in the male than in the female. In the author's series of 103 cases 70 per cent were in males. Innocent tumors may become malignant.

In his earlier experience Fullerton treated all simple papillomas by open operation. He has used transvaginal, transperitoneal and suprapubic extraperitoneal methods of approach. The latter is the method of choice. In villous tumors, diathermy is useful and may be applied through the cystoscope.

In carcinoma of the bladder, results are disappointing. To be of use, resection must be extensive. Radium and deep roentgen rays have not found an important place in treatment in his experience.

Extrophy.—McCarthy and Klemperer⁴³ report a case of malignant disease and extrophy of the bladder. The growth, which was of the cauliflower type, covered the bladder and was treated by diathermy. No attention was paid to either ureteral orifice. The tumor recurred in six months and was again treated with diathermy. One year later there was a second recurrence and it was decided that total cystectomy was necessary. As a preliminary measure bilateral ureterostomy was thought necessary. The right ureter was dilated so that it carried a no. 30 French tube. Later it was found that the left kidney was prac-

42. Fullerton, A.: The Treatment of Bladder Tumors, Irish J. M. Sc., pp. 243-258, June, 1925.

43. McCarthy, J. F., and Klemperer, Paul: Report of Interesting Case of Exstrophic Bladder with Neoplastic Implant, J. Urol. 14:419-427 (Oct.) 1925.

formed unless a protective surface is necessary, gives evidence of the extent of the irritation and trauma. The mucosa of these exstrophied bladders contains areas gradually shading off from fairly normal to definitely malignant tissue. It is of interest that the majority of tumors forming on exstrophied bladder are adenocarcinomas. This is in marked contrast to the types of tumors occurring in normally situated bladders; adenocarcinoma makes up only about 2 per cent of such growths. There were five adenocarcinomas in 333 tumors of the bladder treated at the Mayo Clinic.]

Urinary Retention.—Michon ⁴⁴ reviewed a series of thirty-four cases of urinary retention which occurred in 195 patients who had been operated on for lesions in the lower part of the abdomen. He stated that it is not desirable to carry out the usual repeated evacuation of the bladder by catheter. Many patients who are catheterized are later unable to void normally until they get out of bed, and it is rare to find at that time normal micturition and clear urine. Michon advises two methods of relief for retention. In six cases he gave the patient hexamine which was quite effective in preventing infection. In the remaining cases he injected a solution of boric glycerin into the bladder. Glycerin instillation is quite uncomfortable at times and necessitates catheterization but it usually produces good results and Michon considers it the most desirable method of treating retention.

Voelcker ⁴⁵ comments on the prominence given in recent literature to cicatricial and callous thickening of the neck of the bladder. Often the sound or bougie will show no obstruction to passage but a thickening of the sphincteric region will lead to difficulty in completely emptying the bladder. He feels that the real obstruction to the urine comes from a concomitant thickening of the vesical mucosa adjacent to the thickened sphincter. This protrudes to some extent through the urethral orifice and thus partially cuts off the urinary outlet. Incision of the sphincter by means of a sphincterotome or with the knife by suprapubic incision most frequently leads to cure but some cases require entire excision of the thickened sphincter. Incontinence has not been found to be a complication after such operations. One must assume that the layer of smooth muscle lying next higher comes into function as a sphincter in such cases.

[ED. NOTE.—The type of case mentioned corresponds to contracture of the vesical neck in its various phases. Our attention in this country has been brought to this condition largely through the extensive work

44. Michon, L.: Le traitement de la retention d'urine postoperatoire, Presse méd. 33:1556-1558, 1925.

45. Voelcker, F.: Die Sklerose des Blasenschliessmuskels, Ztschr. f. urol. Chir. 17:103-104, 1925.

of Caulk in this field. The use of the cautery punch as a therapeutic measure is gaining ground and in the majority of such cases seems to produce satisfactory results.]

Extroversion.—Bryan⁴⁶ reports a case of complete extroversion of the bladder in a girl, aged 2½ years. The child had enjoyed good health up to three days before it was seen by Bryan, when while voiding she screamed out with pain. At this time the mother noted a red swelling at the vulva. The family physician reduced this swelling under chloroform anesthesia and told the mother that it was probably the bladder. When seen in hospital the vulva was reddened, some of the veins engorged and the urethra appeared to be dilated. The next day under anesthesia the bladder was washed, a cystoscopic examination made and a cystogram taken. This showed a dilated right ureter which was filled with the cystogram medium. Subsequently the swelling reappeared many times, always in the order of superior wall, followed by the fundus, floor and trigon. Two ureters could be seen on the trigon, a normal left and a dilated slitlike orifice of the right situated quite near the left. After a month of observation and examination it was demonstrated that the bladder was large, thickened, hypertrophied and crisp from repeated hyperengorgements of forcible eversion; the large right pyoureter (associated most likely with an ureterocele) was seen; the right kidney was rudimentary or nonfunctioning and its retention products with that of its ureter were found to be giving rise to severe hyperpyrexia and prostration; the condition of the left kidney was satisfactory and its 80 per cent phenolsulphonphthalein return was thought to justify surgical attack on the right side.

At operation a double kidney was found in the right side, with both ureters dilated. One ureter ended high on the posterior wall of the bladder and the other at the slitlike orifice near the left ureter. The child recovered satisfactorily and at later cystoscopic examinations a cone of ureter was found bulging down from the site of the ureter placed high on the posterior wall. This bulging ureter was the probable exciting cause of the extroversion.

Fistula.—Tant⁴⁷ reports the case of a patient, aged 26 years, who had had an appendectomy and a hysterectomy performed two years previously. Following the operation she rarely urinated normally, most of the urine draining through the vagina. An examination five months after the operation revealed two vesicovaginal fistulas. Cystoscopic examination revealed the two small orifices of the fistula in the region

46. Bryan, R. C.: Complete and Repeated Extroversion of the Bladder Through the Urethra, Associated with Double Right Kidney and Ureter, *J. Urol.* 14:153-181 (Aug.) 1925.

47. Tant: A propos du traitement de la fistule vésico-vaginale, *Bruxelles méd.* 5:1410-1411, 1925

of the left ureteral orifice. The edges of the fistulous tracts were curetted through the vagina, the patient was placed on her abdomen and a permanent urethral catheter inserted. Ten days later, the catheter was removed and no further urine escaped through the fistulas.

Schockaert⁴⁸ reported a case of sigmoidovesical fistula which had been present for twenty-three years, having resulted from a subtotal hysterectomy. Gas and feces passed through the urethra continually and the patient had a severe cystitis and irritation of the external genitalia. The fistula extended deep into the pelvis close to the left ureter. Schockaert did not make a complete dissection of the fistula, as he feared injury to the ureter or a peritoneal infection from opening the sigmoid. A simple ligation of the fistula with silk effected a cure; three years later there had been no further trouble.

Cystitis.—Cairns,⁴⁹ in reviewing eighty cases of cystitis at the London Hospital, found that there were two main clinical types: one in which the disease tended to clear up quickly, either spontaneously or with simple treatment, and the other in which the disease became chronic. In almost all of the chronic cases the cystitis was maintained either by a persistent infection from the kidney or by the presence of residual urine in the bladder. In all the cases there was pus in the urine and the result of bacteriologic investigation showed that colon bacilli occurred with much greater frequency than any other organism. In 35 or 40 per cent of the cases the clinical course indicated that the cystitis was secondary to infection of the kidney or renal pelvis; it was impossible to determine accurately the source of the infection in the other cases. Cystitis of the resolving type was associated with prostatitis in a few instances, but the relationship between these foci of infection was not clear. In some cases the infection undoubtedly came from the kidney, in others possibly from the prostate. There remained, however, many cases in which it was impossible to determine the source of the infection. The chronicity of cystitis is due to a number of conditions. In rare instances it is due to a solitary ulcer of the bladder, a condition of unknown etiology. Usually it is due either to persistent infection from the kidney or to the presence of retained urine in the bladder. A persistent focus of infection in the renal pelvis may give no clinical signs. Evidence obtained by cystoscopy is frequently of great value in the detection of such foci. If the lesion of the renal pelvis is treated efficiently, the cystitis will clear up. Any variety of retention of urine may produce progressive cystitis. The successful treatment depends entirely on the establishment of complete drainage of the bladder either

48. Schockaert, R.: Un cas de fistule sigmoïde-vésicale postopératoire, *Bruxelles méd.* 6:104-105, 1925.

49. Cairns, H. W. B.: Observations on the Etiology and Treatment of Cystitis, *Brit. J. Surg.* 13:78-92 (July) 1925.

Negro's case were: (1) the sex, this lesion being exceptional in women, because of anatomic reasons, and the impossibility of determining whether the lesion had its origin in the intestine or the bladder; (2) whereas feces passed through the urethra, apparently no urine came through the rectum; (3) the erroneous diagnosis, and (4) the useful aid of cystography.

PROSTATE

Prostatectomy.—Delore, Rougemont and Creyssel⁵² state that great benefit is derived from a combined method of the suprapubic and perineal routes in certain cases of prostatectomy, for example when the hypertrophy is excessive and the transvesical extraction requires a fragmentation of the gland or manipulation provoking great trauma or hemorrhage. The perineal stage will thus often be decided on in the course of the operation and only in rare instances will it be decided *a priori* to do the prostatectomy in two stages. This may be indicated if the gland has been inflamed for a long time or submitted to prolonged preliminary radium or roentgen-ray treatment. The authors report the procedures in a case as follows: (1) fruitless attempt of hypogastric enucleation; (2) the suprapubic route momentarily abandoned; the perineal region prepared, the perineum incised either medially or transversely and the perirectal space separated, and a small opening made in the urethra at the level of the prostatic end and the finger inserted in that opening; (3) by combined manipulation, of the abdominal and perineal fingers, extraction of the prostate through the abdominal incision, and (4) warm lavage and continuous through and through drainage, the drain being removed on the third day and replaced by a retention catheter. The perineal incision heals readily and the postoperative course is similar to that of a simple suprapubic operation.

[ED. NOTE.—It is only rarely that a perineal incision is necessary. If it is necessary to elevate the prostate from below it can readily be reached from its rectal surface.]

Salvini⁵³ reviews 180 cases in which suprapubic prostatectomy was performed by Professor Marion in the Service Civile during a period of about three years. There were thirteen deaths, a mortality rate of 7.2 per cent. There was one serious case of peritoneal infection, eight cases of marked hemorrhage, occurring within three days after operation,

52. Delore, X.: De Rougemont, J., and Creyssel, J.: De l'utilité de la voie combinée hypogastrique et périnéales dans certaines prostatectomies difficiles, J. d'urol. med. et chir. 19:398-401, 1925.

53. Salvini, P.: Resultats immédiats et éloignés de la prostatectomie sus-pubienne chez 180 malades opérés de 1921 au 30 Juin, 1924, J. d'urol. med. et chir. 20:103-124, 1925.

two cases of tearing of the membranous urethra with late formation of a urethral stricture and two cases of infected wound. There were two cases of epididymitis, either an exacerbation of a previously existing infection, or, as Marion thinks, a condition due to a failure to section the vas, a practice he performs in every case of prostatectomy in order to avoid epididymitis. In sixteen of the 180 cases the fistula had to be closed surgically; Marion states that fistulas that do not close in thirty-five days after operation should be resected, liberated from the edges of the bladder and sutured in three layers. There were two cases of phlebitis. In two cases the passage of the catheter was difficult, and in two cases it was impossible on account of scarring of the vesical extremity of the urethra. In both cases Marion had to reestablish the permeability by the use of a *béniqué* sound guided by one finger introduced into the prostatic cavity through the suprapubic wound. All the patients after removal of the permanent catheter were able to void. In fifty-seven cases further catheterization had to be done, in forty-two the bladder was emptied completely and in fifteen partially, with a residue of urine varying from 20 to 225 cc. The urine began to clear usually from ten to twenty days after operation. Late results were obtainable in 148 cases; in eleven micturition was slightly painful, in none had the catheter been used, in 144 there was night frequency, in thirteen residual urine varying from 30 to 90 cc., and in nineteen there was cloudy urine. In twenty-five sexual function had diminished; all the patients were more than sixty-two years. Three patients developed urinary calculi; two of these had had stones before operation. Four patients had incruusted cystitis; a perfect cure was obtained by suprapubic curettage. The few patients who were incontinent after removal of the catheter recovered normal function following urethral dilatation. Salvini states that prostatectomy influences the bladder favorably but that it does not aid in the regression of any disease of the kidney. Dysuria disappears, but polyuria continues. Two patients died a few months after operation from interstitial nephritis. Only eight patients did not improve in general health; they had had partial retention of long standing before operation. One patient who had had several attacks of epilepsy was cured after prostatectomy. One patient committed suicide; Marion has noted several cases of neurasthenia following prostatectomy.

Michon⁵⁴ reports on the benefits and the inconveniences of the two-stage prostatectomy. The first stage of the operation releases the vesical distention which destroys renal function, and also reduces the vesical infection and the later operative risk. Chronic retention frequently causes distention which also affects the kidney and produces a toxemic

54. Michon, E.: *De la prostatectomie en deux temps*, Semaine d. hôp. de Paris 2:47-50, 1925.

state with high urea retention. In order to reduce this primary distention one of two procedures may be followed, catheterization or suprapubic drainage. Catheterization must be repeated frequently and often causes a dangerous infection; suprapubic drainage, done under local anesthesia, with gradual emptying of the bladder, is less likely to cause infection. From several weeks to several months should elapse between the two stages. If infection or calculi are present suprapubic drainage is the only satisfactory procedure. The inconvenience of the two-stage operation is primarily the greater difficulty in removing the prostate at the second stage as the plane of cleavage has partly disappeared, and if the drainage has been maintained for a long period of time the fistulous tract has become thickened and fibrous and it is necessary to resect the fistula in order to obtain a good closure of the bladder. With the two-stage operation the patient is incapacitated for a much longer period. Michon concludes that if the patients are young, have normal blood urea, and have no infection or only slight infection, the one-stage operation is the more satisfactory.

[ED. NOTE.—Table 3 taken from the recent report of Liebig⁵⁵ is interesting in regard to the mortality in one and two-stage suprapubic operations.

TABLE 3.—*Mortality in One and Two-Stage Suprapubic Operations (Liebig)*

| Suprapubic (one-stage) | Number | Deaths | Per Cent |
|------------------------|--------|--------|----------|
| 1912 to 1916..... | 2,958 | 248 | 8.38 |
| 1917 to 1922..... | 2,379 | 189 | 7.9 |
| | 5,337 | 437 | 8.1 |
| Suprapubic (two-stage) | | | |
| 1912 to 1916..... | 276 | 28 | 10.2 |
| 1917 to 1922..... | 507 | 22 | 4.3 |
| | 783 | 50 | 6.3 |

Unquestionably the two-stage operation reduces the operative risk, the hemorrhage usually occurring with prostatectomy is much less and the organism has had time to readjust itself to a new condition of drainage and exposure before the more serious procedure of removal of the gland is performed. One of the most important features of a preliminary drainage is that the patient develops at least partial immunity to his own type of colon bacillus infection; after the second operation if a cysto-ureteropyelonephritis develops it is usually mild and the patient is, with his increased resistance, well able to stand the infection.]

55. Liebig, Fritz: Die Prostatahypertrophie, Ztschr. f. Urol. 17:593-613; 625-659, 1923.

Postoperative Hemorrhage.—Leguen and Garcin⁵⁶ state that the onset of postoperative hemorrhage following suprapubic prostatectomy may occur from two to three or four days after operation; rarely it may occur on the tenth or twelfth day. The hemorrhage may be due to several factors, such as the size of the adenoma; the large easily enucleated tumors bleed readily. The type of the operation also is important; there is much less bleeding in the two-stage operation, especially if a long, closed lap has elapsed between the two operations. Ether and gas are likely to cause hemorrhage during the operation; chloroform causes less and apparently spinal anesthesia markedly reduces the amount of hemorrhage during the operation. On the other hand spinal anesthesia often provokes delayed hemorrhage several hours after operation on account of a labor or secondary exsanguination. Local anesthesia does not affect loss of blood. In none of Leguen's cases the prostatic cavity was packed after operation, this has several disadvantages as there is considerable pain connected with a distention of the cavity and with removal of the packing and also the danger of infection is increased on account of the irregularity and power of absorption of the lacerated prostatic bed. Hemostasis is not perfect in a packed wound as a small clot of blood may be disturbed in withdrawing the strip of gauze and cause a new hemorrhage. Because of this Leguen and Garcin have recently tried a new method of controlling hemorrhage; they endeavored to increase the coagulating power of the blood. The work is based on the fact that after prostatectomy the blood has the same consistency and follows the same course as it does following any severe hemorrhage; it passes through a period of hypocoagulability lasting from four to five days and is followed by a period of hypercoagulability lasting from three to four weeks and reaching its acme on the ninth day after operation. They tried injections of a proprietary drug that increases the coagulation of the blood, which definitely reduced the hemorrhage and allowed the removal of packing on the second or third day; they also used calcium chloride in 5 per cent solutions, injecting from 10 to 20 cc. before operation. The results were satisfactory in ten cases in which packing was not necessary. In two other cases the results were unsatisfactory. At present Leguen and Garcin use the following technic: Five days before operation a daily injection of 10 cc. of a 5 per cent solution of calcium chloride, and two days before operation a daily intramuscular injection of 10 cc. of the proprietary drug mentioned also is given. Thirty prostatic cases have been treated with success in this manner; it was not necessary to use packing in any case.

⁵⁶ Leguen, R., and Garcin, A.: Le traitement preventif des hemorrhagies dans la prostatectomie transvesicale, *Semaine d. hôp. de Paris* 2:41-45, 1925.

Prostatitis.—Belostozky⁵⁷ reviews the literature on the development of our knowledge of acute prostatitis and quotes the work of Segond, Desault and Petit, Lallemand, Dugas, Begin, Velpeau and others on the pathology of the condition.

While the possibility of aseptic prostatic abscess is not to be denied, in by far the greater number of cases pathogenic organisms are the inciting cause. Of these the gonococcus takes first place. However, the other pyogenic organisms, such as the staphylococcus, streptococcus and colon bacillus, may by themselves or, more frequently, in association with the gonococcus, produce the condition. Staphylococcus and streptococcus prostatitis not associated with gonococcal infection are not infrequent; Belostozky cites a number of such instances. Segond found no disease in the posterior urethra in twelve of 115 cases, while Belostozky found the posterior urethra uninvolved in only five of seventy cases. Metastatic prostatic abscess occurs rarely. Of etiologic moment may be mentioned severe physical work, chilling, excessive sexual indulgences, irritation from riding and the like, but these are to be considered predisposing rather than direct causes. Not infrequently prostatic abscess may develop from forced urethral irrigation or instrumentation. Three symptoms are constantly observed, prostatic enlargement by rectal palpation, pain in the anal region and difficulty in urination. In twenty-one of the seventy cases there was complete urinary obstruction so that the catheter had to be used. Eighteen of the seventy cases ran an afebrile course. There was no relation between the severity of the course of the disease and the size of the abscess. In forty of the cases the disease subsided by rupture of the abscess into the urethra or the rectum. Some authors hold that this is practically always the mode of spontaneous cure. The abscess ruptured into the urethra in twenty cases, into the rectum in ten, and into both in three. The prognosis, so far as life is concerned, is good. None of the author's seventy patients died. Fistula formation is frequent. Two recto-urethral fistulas in the series healed spontaneously in a short time. The disease lasted an average of thirty days.

Conservative treatment consists in hot applications, rest, milk injection and vaccine. Gentle prostatic massage is undertaken after the abscess has begun to subside. Statistics show that the mortality when operation is performed runs higher than when conservative treatment is carried out. Belostozky operated on eight patients by drainage through a prerectal incision with good results. He feels that operation should be reserved for cases of such persistence or severity as will not respond

57. Belostozky, M.: 70 Fälle akuter eitriger Prostatitis, *Ztschr. f. urol. Chir.* 17:53-60, 1925.

to conservative methods. Emphasis is placed on the good results to be obtained from injections of milk (nonspecific protein therapy).

[**ED. NOTE.**—The emphasis of persistent application of conservative measures in acute prostatic abscess rather than hurried operation corresponds to the usual urologic teaching in America. In certain cases nonspecific protein therapy gives brilliant results, but this is not consistent. However, if complete urinary retention is not relieved in a few days, if fever persists with recurrent chills, operation is indicated. Many surgeons still hold to perineal urethrotomy with breaking into the abscess through the prostatic urethra and subsequent perineal drainage of the prostatic urethra and bladder with an indwelling catheter.]

Leguen⁵⁸ states that while performing prostatectomy for adenoma one occasionally encounters a suppurative infection of the prostate; the infected section usually is soft and spongy and may contain pure staphylococci. The extent of the infection is, in a certain way, proportional to the volume of the tumor. It is situated in the prostatic tissue as well as in the adenoma, but its origin is always in the tumor itself and as soon as the latter is removed infection ceases. This condition may be secondary to a localized area of infection, especially in the skin. Catheterization may cause it, but in most cases the catheterization is necessitated by retention due to an unsuspected infection. The presence of the adenoma may cause the infection or it may develop during the course of a cystostomy. Leguen divides the infected prostatic adenomas from a clinical standpoint into three groups. The most common type is a simple prostatic suppuration: when this is the case the abscess must be opened through the perineum or an immediate prostatectomy may be performed, but this is undesirable. Leguen drains the abscess through the perineum, vaccinating the patient against his infection and then performing secondary prostatectomy. A second type of case is characterized by fever without suppuration. This type includes the patients with acute retention accompanied by a fever which is usually attributed to catheter infection but is really due to an infected adenoma.

In the same group are patients who have had cystostomy performed and develop fever several weeks or months after operation. Cystostomy is not always the cause of the fever in these cases; there may have been an infected adenoma present before operation, and in such case it is better to wait and operate when all symptoms of infection have subsided, although sometimes surgical intervention is necessary on account of a persistent fever, in which case the removal of infected adenomas may bring about a complete cure. Leguen has reported cases in which this infection had invaded the pelvis and caused pericystitis. In the third

58. Leguen: Les infections de l'adenome prostatique, *Le Monde médical*, 1925, pp. 297-303.

type a partial or total induration of the prostate may be found. On account of the hardness of the prostate the condition is thought to be malignant, but there is less induration in the region of the seminal vesicles than occurs with cancer, and eosinophilia may be present. In these cases a two-stage prostatectomy should be done which permits the prostate to regress after cystostomy and at the same time affords an opportunity to improve the patient's general health before the gland is removed.

Blanc ⁵⁹ states that patients with enlarged prostates and infected urine should be divided into two groups, those who have been catheterized and those who have not. If the patient has not been catheterized and the enlargement of the prostate is of recent origin, the urine should be clear; if it is not, some other part of the urinary tract is affected. If the enlargement is old and there is some residual urine, although the colon bacillus frequently provokes chronic cystitis, the pyuria should be considered as evidence of some other lesion. If the patient has been catheterized the chances are, especially if he has been frequently catheterized, that he has an infected prostate, but if the catheter has only been occasionally passed and the urine is very purulent, vesical or renal lesions must be thought of. Blanc reports nine cases of prostatic infection with pyuria, in which there were also renal and vesical calculi, large ureters, diverticula and renal and prostatic tuberculosis.

TESTIS

Tumors.—Bell ⁶⁰ studied fifty specimens of tumors of the testis. These represent most of the various types of testicular tumors commonly described but thus far there has been little unanimity of opinion as to their proper classification and origin. In Bell's series most of the tumors fell into two main groups, the teratoid and the germinal cell. The latter group has been variously designated germinal cell carcinoma, seminoma, spermatocytoma, embryonal carcinoma and round cell sarcoma. The teratoid group predominated to a marked degree. In this group perhaps the most popular of the various designations has been fibrocystic disease, a term justified by the naked eye and lower magnification appearance of cysts supported by a matrix of fibrous tissue. Various other terms, such as chondroma, chondrosarcoma, chondro-adenoma, osteoma, adenoma, squamous cell and columnar cell carcinoma, are referable to the most obvious histologic features, occasionally displayed, which have dominated the mind of the pathologist. These older terms serve as an indication of the remarkable structural varia-

59. Blanc, H.: La pyurie chez les prostatiques, *J. d'urol. med. et chir.* **19**: 506-512, 1925.

60. Bell, F. G.: Tumours of the Testicle: The Teratoid Group, *Brit. J. Surg.* **13**:738 (July) 1925.

tions presented by these tumors, which are now regarded as variations from a common teratoid basis. These tumors vary greatly in size, shape and consistency. The internal structure is best demonstrated by sagittal section, which brings out the relation of the tumor to the body of the testis and to the epididymis, and may, in early specimens, clearly demonstrate its frequent origin from the mediastinum testis. In the early stages the body of the testis is usually visible to the naked eye at some part of the periphery of the tumor, commonly at the summit, and may be fairly normal in shape and size, while in large tumors it undergoes progressive compression till it is reduced to a narrow straplike peripheral layer only detectable under the microscope. The presence of a peripheral band of testicular tissue separated from the substance of the tumor by a condensed fibrous layer or capsule is highly characteristic of teratoma, but not pathognomonic. Many specimens are cystic, and some are cartilaginous. Teratoma of the testis displays histologic characters of a highly variable complexity, and the individual representation of the blastodermic layers varies greatly in different specimens. After examining a considerable number of these tumors it is possible to reduce them to a group type. A brief description is as follows:

Mesoblastic Derivatives: The presence of cartilage in the form of round or oval nodules or crescentic plates is characteristic. A fibrocellular myxomatous matrix, sometimes sarcomatous, is almost equally characteristic and always suggests that any tumor under consideration is teratoid in character.

Hypoblastic Derivatives: These take the form of tubules or spaces lined by cubical or columnar cells, often suggesting the glandular structures in adults, especially intestinal mucosa.

Epiblastic Derivatives: These take the form of spaces lined by stratified squamous epithelium, and cell nest formation is often a striking feature.

Metastasis may take place by the lymphatics, the blood, or both, depending on the predominance or admixture of carcinomatous or sarcomatous elements. It is also possible that transplantation of fragments of tumor may take place from comparatively innocent tumors, such as the chondromatous teratoma, by direct invasion of venous channels. Paget's enchondroma is often regarded as an example of this, and the secondary tumors in the lung, as produced by transplantation after erosion of the spermatic vein.

Hinman, Gibson and Kutzmann⁶¹ report in detail twenty-two cases of malignant tumor of the testis. Ten were diagnosed teratomas or mixed tumors and twelve as seminomas or single cell tumors. Sarcoma

61. Hinman, Frank; Gibson, T. E., and Kutzmann, A. A.: Malignant Tumors of the Testicle; a Pathological Study, *Ann. Surg.* 82:552-575 (Oct.) 1925.

of the testis is rare; there were none in this series. All the tumors were malignant. Hinman asserts that practically all tumors of the testis are teratomatous in origin, and that practically all exhibit some type of carcinomatous degeneration of which the so-called seminoma is but a modification. Clinically it is now fairly well established that the seminoma is relatively susceptible to radiotherapy, whereas other types of teratoma are less favorably influenced.

Triorchidism.—Holder⁶² stated that proved cases of triorchidism are rare. He reports the case of one in a man, aged 45, whose chief complaint was pain in the left inguinal region. Physical examination led to a provisional diagnosis of cellulitis of the affected tissues, or adenitis of the inguinal lymph nodes. After twenty-four hours' observation the area was incised and pus evacuated. On the eighteenth day, the patient having grown worse, the "infected glands" were removed. Examination of the tissue removed showed differentiated testicular tissue, vas deferens and epididymus. As there were two normally placed testes in the scrotum, Holder seems to be justified in assuming this to be a case of triorchidism. It is probably the second case to be reported of a third functioning testis.

URETHRA

Tuberculosis.—Minet in 1910 could find only seven cases of tuberculosis of the urethra reported in the literature. Boeckel and Oberling⁶³ reported a case of a man, aged 35, who was sent to them to be treated for urethritis. He had had pulmonary tuberculosis. The lesion of the urethra had been noted four months before, starting with a sudden urethral discharge followed two weeks later by swelling, without apparent sign of inflammation, in the right perineal region. Gonococci were found in the urethral discharge. Potassium permanganate solution was injected but without success. The swelling increased, forming a mass measuring about 7 by 7 cm. below the prostate; it was adherent to the deeper tissues. Cystoscopic examination of the prostate and bladder was negative. The mass was excised; it contained bacilli of tuberculosis. Some of the urethral discharge injected into a guinea-pig produced tuberculous lesions. A few weeks later, definite tuberculous granulations appeared in the urethra. The patient died subsequently of pulmonary tuberculosis. Postmortem examination revealed the presence of nodular fibrous tubercles of the urethra, there were also a peri-urethral abscess and a prostatic abscess that was completely isolated

62. Holder, H. G.: A Probable Case of Triorchidism, *J. Urol.* **13**:555-564 (May) 1925.

63. Boeckel, André; and Oberling, C.: Un cas de tuberculose de l'urethre, *J. d'urol. med. et chir.* **19**:127-131, 1925.

from the urethra, a few tuberculous ulcerations in the bladder and, finally, a beginning caseous tuberculosis of the left kidney. These lesions evidently had their origin in the pulmonary tuberculosis. The renal and vesical lesions were recent, independent of the urethral and periurethral lesions. The prostatic abscess probably also formed afterward. These facts were established both clinically and pathologically. The periurethral mass removed at operation was an old lesion, which certainly preceded the symptoms of urethritis. There was a urethral stricture present, probably caused at first by the periurethral mass; it was relieved only partially by removal of the tumor. At necropsy it was found that there was also an area of tuberculous narrowing of the urethra, a fibrous lesion of the urethral wall itself which was covered with tuberculous nodules.

Valvular Obstruction.—Hinman and Kutzmann⁶⁴ report six cases of congenital valvular obstruction of the posterior urethra and review fifty cases from the literature. They find that such obstruction occurs mainly in early boyhood, most of the cases (62 per cent) occurring prior to the age of 10 years, and is serious because irremediable pressure changes may have already occurred or recognition of the obstruction be delayed during childhood beyond the period when intervention could cure the disease. It is probably more common than the few reported cases indicate, and this tardy recognition of a condition so often fatal warrants recording their six cases, with a full discussion of cases reported by others. The importance of a knowledge of the obstruction by the practitioner and pediatrician, on whom the first responsibility of diagnosis rests, is apparent in view of the ease with which it can be recognized cystoscopically and the great benefit of early treatment.

The condition has been recognized for more than a century but it is only recently that correct diagnoses have been made during life. The etiology is still a matter of conjecture. Occurrence of the obstruction in the stillborn and in young infants points strongly to an embryologic basis. The early symptoms are chiefly those of urinary obstruction and infection; later, renal insufficiency occurs. A correct diagnosis is possible only after careful history taking and a thorough urologic investigation which may include cysto-urethroscopy, urography and a study of renal function. A clinical diagnosis was made in six cases reported by the authors.

The treatment is not difficult and consists in the destruction of the valves by fulguration through the cystoscope or by radical surgical intervention suprapubically or perineally or by combining the two methods of approach.

64. Hinman, Frank; and Kutzmann, A. A.: Congenital Valvular Obstruction of the Posterior Urethra, *J. Urol.* **14**:71-112 (Aug.) 1925.

The early incidence of the condition, its insidious nature, gradually causing, as it does, serious renal damage that may soon become irremediable and result fatally; its recognition by proper methods of examination and the fact that if recognized early it can be easily cured emphasize the extreme clinical importance of congenital valvular obstructions of the posterior urethra.

Huddy⁶⁵ classifies urethral pouches as congenital or acquired. The acquired type may be caused by dilatation or perforation of the urethra from stricture, calculus, injury or infection. The pouches vary greatly in size but those giving rise to symptoms are usually about 3.5 cm. in diameter. Sisk is quoted as saying that only eighty cases have been reported in the literature; this, however, probably exaggerates their rarity. Many hypotheses have been advanced to explain the origin of the congenital pouch. As the cavity is found on the ventral aspect of the urethra, two explanations are imperfect fusion of the two genital folds and the fact that one of the cystic epithelial ducts may retain its urethral communication and become dilated. Some of the pouches, however, may arise from the müllerian ducts, but these are probably very rare. Clinically, urethral pouches are of two types. In the first type the patient presents himself with rather vague and indefinite symptoms, and a diagnosis can be made only by means of the urethroscope. In the second type swelling at some point along the urethra is found.

URINARY INFECTION

Shaw and Hill⁶⁶ report an epidemic of thirty-six cases of wound infection, observed in the urologic wards of the Johns Hopkins Hospital. The infection occurred only in wounds that were the site of urinary drainage. In thirty-four cases it followed perineal prostatectomy and in two cases occurred in suprapubic wounds. The appearance of the lesions clinically and the course of the infection were characteristic. The essential features were: pain in the incision, a rolled-up appearance of the skin margin, and the formation of a dirty gray membrane that would subsequently become black and slough. Invariably the wounds gave off a strong ammoniacal odor. In untreated cases the membrane often reformed and the process repeated itself. There was little or no constitutional reaction. The temperature usually remained normal and the leukocyte count rarely exceeded 10,000. The wounds were painful and frequently opiates were necessary. The etiologic organism was a gram-positive bacillus with some cultural characteristics similar to the

65. Huddy, G. P. B.: Urethral Pouches, *Brit. J. Surg.* **13**:50-57 (July) 1925.

66. Shaw, E. C., and Hill, J. H.: Report of a New Pathogenic Organism (*Corynebacterium Thompsoni*) with Description of an Epidemic of Infection of Urinary Fistula, *J. Urol.* **13**:689-713 (June) 1925.

diphtheria bacillus, but differing from it in certain morphologic features and in pathogenicity. The authors have proposed the name of *Corynebacterium thompsoni* for this species. The organism was seen in direct smears from the lesions and obtained by culture in every case that showed the infection clinically. On making cultures from the hands of all those coming in contact with the patient, it was found that the infection was propagated by the orderlies. The usual antiseptics were useless in combating the infection. Most of the cases cleared up promptly under local application of 5 per cent acetic acid, and by spraying the wounds of the patients with 1 per cent acetic acid solution infection was prevented. The etiologic organism was studied in reference to its pathogenicity for rabbits and guinea-pigs. It was found impossible to infect the normal urethral mucous membrane of rabbits by injections of cultures or to infect surface wounds that were not draining urine. After producing a suprapubic urinary fistula, however, inoculation was invariably successful, being followed by the appearance of the same type of lesion that occurred in man. The organism was recovered by culture in every case. These lesions did not occur in uninoculated urinary fistulas or in those inoculated with proteus.

[ED. NOTE.—Two cases have occurred in the urologic wards of St. Michael's Hospital, Toronto, within the last year, which appeared and behaved clinically like those described by Shaw and Hill. The first case was that in which a two stage suprapubic prostatectomy had been performed and this type of infection occurred after the primary drainage. After a prolonged course it cleared up only to recur after the prostatectomy was performed. The patient recovered after a stormy convalescence but has a hernia. The second infection occurred after primary suprapubic prostatectomy; unfortunately the causative organism was not isolated, but otherwise the case resembled in every respect those described by Shaw and Hill. Recovery was spontaneous although protracted. The two patients were not in the hospital at the same time.]

Henline,⁶⁷ after a review of fifty cases of urinary infection treated with hexylresorcinol, asserted that careful urologic examination should be made of all such infections before treatment is instituted. Such examinations should include cultures, tests of renal function and roentgenograms. Hexylresorcinol is a superior urinary antiseptic, as it may be administered by mouth and is nonirritating to the urinary tract. It is bactericidal for all organisms infecting the urinary tract. An average of sixty-three days for *Bacillus coli*, eighteen days for *Staphylococcus aureus*, ninety-four days for *Bacillus proteus*, ninety-one days for *Bacillus lactis-aërogenes*, and 133 days for mixed infections, was neces-

67. Henline, R. B.: Hexylresorcinol in the Treatment of Fifty Cases of Infections of the Urinary Tract, J. Urol. 14:119-133 (Aug.) 1925.

sary to sterilize the urine. Only one case recurred, and in this one treatment was discontinued too soon. Ninety-two per cent of the patients were cured. Of the three that were not cured, one did not return for treatment, one still had a growth of *Bacillus fluorescens*, and one had a tumor of the bladder as a complication. These three are cured clinically.

Henline suggests that the drug may be useful in preventing recurrence of stones, and in the healing of sinuses if there is streptococcal infection.

Scott and Hill,⁶⁸ after extensive investigation of the subject of preoperative skin disinfectant in which comparative studies were made as to the value of several substances in general use and considered relatively satisfactory, conclude that an alcohol-acetone-aqueous solution of mercurochrome is most effective. This solution is made by dissolving 2 Gm. of mercurochrome in 35 cc. of distilled water and then adding 55 cc. of 95 per cent alcohol solution and 10 cc. of acetone. This solution is found to be more efficient than tincture of iodine, potassium mercuric iodide or picric acid. It is particularly valuable in local anesthesia because its application is entirely painless and does not cause local dermatitis. It penetrates as deeply as does picric acid and more deeply than iodine or potassium mercuric iodide. The solution is quite stable and retains its bactericidal power for at least forty-six days. Its color serves as a useful guide as to the thoroughness of the preparation. Its toxicity is low.

68. Scott, W. W., and Hill, J. H.: Presentation of a Preoperative Skin Disinfectant, an Alcohol-Acetone-Aqueous Solution of Mercurochrome, *J. Urol.* **14**: 135-152 (Aug.) 1925.

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MUSCULAR RIGIDITY WITH AND WITHOUT SYMPATHETIC INNERVATION*

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The old question of the influence of sympathetic nerve fibers on the so-called tonus of skeletal muscle has recently attracted renewed attention, in view of a somewhat widespread agitation for surgical relief of spastic paralysis by "ramisection." A great deal of experimental work has been directed to this problem, and a still larger amount of speculation has been expended on it. Yet the problem seems to be still in a decidedly unsettled state.

So much of the previous work has been inconclusive and so conflicting has been the testimony that we have attempted to clarify the subject by emphasizing quantitative methods of experimentation, by searching carefully for all possible sources of experimental error, and by critically examining our results and the various arguments in the light of modern knowledge of nerve-muscle physiology. Perhaps the chief justification for adding to the already heavily burdened literature of the subject is the uncertainty in the minds of many surgeons as to whether or not the operation of ramisection is advisable for their patients.

The literature of the subject has recently been admirably reviewed by Cobb.¹ The salient points may here be summarized. The basis of the argument for this operation to relieve spastic paralysis seems to be, in the first place, the anatomic observation by Boeke² apparently showing that skeletal muscle fibers are innervated by sympathetic as well as by cerebrospinal nerve fibers. This observation naturally led to a search

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1. Cobb, S.: *Physiol. Rev.* 5:518 (Oct.) 1925.

2. Boeke, J.: *Internat. Monatschr. f. Anat. u. Physiol.* 28:377, 1911. Boeke, J., and Dusser de Barenne, J. G.: *Proc. Sect. Sc. Wet. Amsterdam* 21:1227, 1919.

for the functional significance of the sympathetic fibers, and, on cutting these in frogs, De Boer³ found a loss of "tone." On the strength of these observations Langelaan⁴ built a theory that "contractile tonus" (by which the limb assumes a posture) depends on the cerebrospinal nerve fibers, and "plastic tonus" (by which the limb maintains a posture already assumed) depends on the sympathetic fibers. He performed experiments purporting to differentiate between plasticity and contractility as muscular functions. In support of his views he cited Sherrington's observation⁵ on "plastic tonus," i. e., the "lengthening" and "shortening" reactions whereby in the decerebrate mammal the limb, when passively extended or flexed, tends to remain in the posture imposed. More recently Hunter,⁶ assuming Langelaan's theory to be valid, performed experiments in which he claimed to have shown that cutting the sympathetic fibers destroys the plastic element in tonus, leaving the contractile element unimpaired. On the strength of these observations Royle⁷ undertook to introduce the operation of ramisection with the idea that, by removing the plastic element in tonus, relief of the condition of spastic paralysis would be effected. Coombs and Tulgan⁸ and also Kuntz and Kerper⁹ have recently reported a few observations on cats tending to support Hunter's view.

Both Cobb¹⁰ and Dusser de Barenne,¹¹ seeking to test the question by critical experiment, were unable to find any influence of sympathetic nerves on tonus in skeletal muscles, decerebrate or otherwise. Several other investigators, notably Kanavel, Pollock and Davis,¹² have likewise failed to substantiate De Boer's results. Since the completion of our experiments, a report has appeared of a similar series on dogs by Meek and Crawford,¹³ corroborating the work of Cobb in showing the absence of any demonstrable influence of sympathetic nerves on tonus in the limb muscles. Therefore, the bulk of experimental evidence

3. De Boer, S.: *Ztschr. f. Biol.* **65**:239, 1915.

4. Langelaan, J. W.: *Brain* **38**:235, 1915.

5. Sherrington, C. S.: *Quart. J. Exper. Physiol.* **2**:109, 1909.

6. Hunter, J. I.: *Surg. Gynec. Obst.* **39**:721 (Dec.) 1924; *Am. J. M. Sc.* **170**:469 (Oct.) 1925.

7. Royle, N. D.: *Surg. Gynec. Obst.* **39**:701 (Dec.) 1924.

8. Coombs, H. C., and Tulgan, J.: *Am. J. Physiol.* **74**:314 (Oct.) 1925.

9. Kuntz, A., and Kerper, A. H.: *Proc. Soc. Exper. Biol. & Med.* **23**:77, 1925.

10. Cobb, S.: *Am. J. Physiol.* **46**:478 (July) 1918.

11. Dusser de Barenne, J. G.: *Folia neuro-biol.* **7**:651, 1913.

12. Kanavel, A. B.; Pollock, L. J., and Davis, L. E.: *Experimental and Clinical Experiences with Sympathectomy in Spastic Paralysis*, *J. A. M. A.* **83**:1615 (Nov. 15) 1924.

13. Meek, W. J., and Crawford, A. S.: *Am. J. Physiol.* **74**:285 (Oct.) 1925.

seems to be against the view that sympathetic nerve fibers contribute directly to tonus in skeletal muscle.

Hunter¹⁴ made answer to the negative findings of Cobb and Dusser de Barenne by emphasizing the distinction made by Langelaan between plastic and contractile tonus. He assigned to the coarser muscle fibers, innervated by cerebrospinal nerve fibers, the function of contraction; and to the more slender fibers, innervated, according to Kulchitsky,¹⁵ by sympathetic nerve fibers, a function similar to that of the molluscan "catch" muscle; viz., the ability to maintain posture already imposed either passively or by contraction of the coarser fibers (comparison should be made with observations of Needham¹⁶). He ascribed the negative results of other workers to the failure to recognize the presence or absence of "plastic" tonus, for he contended that this and only this element is abolished by cutting the sympathetic fibers. Decerebrate rigidity, he said, will still be present, for it depends, in part, on the contractile function. The experiment must be especially designed to show the presence of the plastic element in tonus; lengthening and shortening reactions and the ability to maintain posture against the force of gravity should be especially noted as evidence to show whether or not the plastic function has been disturbed.

Cobb has shown in his review¹ that Langelaan's theory is without real foundation, in that no crucial evidence has been brought forward to prove the existence of any two such elements in tonus as he assumes. It should be noticed that Sherrington never maintained that plasticity was a separate function from contractility in tonus. He merely called attention to the superficial similarity between the plastic decerebrate limb and the adductor apparatus of the mollusk, in the ability of the muscle in each case to maintain a given degree of shortening irrespective of the amount of tension. He also furnished evidence tending to show that this behavior was due to proprioceptive reflexes; i. e., reflexes initiated by afferent impulses arising within the muscle involved. But he made no assumption as to the type of motor-nerve fibers or of muscle fibers involved, merely noting the striking degree of plasticity conferred on the limb by its proprioceptive reflexes.

Two considerations derived from our experience throw doubt on the existence of these alleged functionally distinct elements in tonus, the plastic and the contractile, and especially on the view that they are relegated to distinct neuromuscular mechanisms.

1. In observing more than 200 decerebrate cats, in the course of a variety of researches on spinal reflexes, we have seen all grades of

14. Hunter (footnote 6, second reference).

15. Kulchitsky, N.: J. Anat. 58:152, 1924.

16. Needham, D. M.: Physiol. Rev. 6:1, 1926.

decerebrate rigidity from extreme extension strongly maintained, on the one hand, to complete flaccidity, on the other. When rigidity is extreme it is difficult to force passive flexion, and the tendency to return to full extension is so great that it is difficult to obtain the lengthening reaction. When the rigidity is weak there is not enough tonic activity to show the plastic effects to advantage. Therefore, these reactions of plastic tonus are best revealed in the intermediate state of moderate rigidity. We have seen nothing that suggests any other determining condition for plasticity than a moderate degree of decerebrate rigidity. The plastic reactions seem to be more simply explained, as suggested by Sherrington, through the operation of proprioceptive (myotatic) reflexes, the end organ being the contractile muscle innervated by cerebrospinal nerve fibers, than by invoking a special plastic mechanism in the muscle. Indeed, since decerebrate rigidity is marked by action currents indistinguishable in form and rhythm from those in other sustained contractions, we see no reason to suppose that tonus in skeletal muscle involves any function fundamentally different from any other contraction.

2. It is difficult to reconcile the alleged plastic function of the sympathetic nerves with the known facts of nerve-muscle physiology. Before nerve physiology had reached its present state it was customary to think of the nerve trunk as if it were a wire carrying an electric current, or a pipe conducting a stream of fluid, and to treat stimulation as if it set up a steady stream of energy which could be graded in amount or intensity without limitation. We now know that the stream of nervous energy, however initiated, consists in individual nerve impulses, each impulse in a single nerve fiber being a brief, transient event, of explosive character, in that it exhausts all the energy available at the moment, and therefore obeys the all-or-nothing law. Thus, instead of a steady stream of nervous energy, we have a sequence of separate impulses whose frequency is limited by the refractory period of the conducting fiber.¹⁷ Now Langelaan's theory, on which Hunter and Royle base their work, holds that plastic tonus is controlled by the sympathetic nerve fibers, which implies that motor impulses in these fibers initiate this function in the muscle fibers. Indeed, we know of no influence conveyed by nerves, other than nerve impulses, which could evoke any sort of functional response in muscle. All experimental evidence points to the view that the functional response in a given excitable tissue, nerve or muscle, is of one kind; i. e., no qualitative differences are possible in the nerve impulse, nor in the corresponding response of a given muscle fiber. The quantitative differences in the activity of a given tissue depend solely on the number of functional

17. Lucas, K.: *The Conduction of the Nervous Impulse*, London, 1917.

units (fibers) excited and on the number of individual responses evoked in each fiber in a given time, and, in the case of muscle, on the load encountered.¹⁸ Furthermore, the properties of all skeletal muscles seem to be such that functional response always results in contractile effort. The quickness and strength of contraction may differ enormously in different types of muscle, but all are alike in their tendency to contract on excitation, and excitation of skeletal muscle by the nerve impulse evokes the same type of response as direct artificial excitation. Therefore, all the evidence now known fails to show how sympathetic nerve fibers could convey messages to skeletal muscle fibers, telling them to hold their length unchanged, without releasing contractile energy in them.

It is true that the molluscan adductor muscle, which has served in the literature¹⁹ as the prototype of plastic tonus, presents a behavior apparently as difficult to explain in terms of individual functional response as the alleged plasticity in mammalian skeletal muscles. The "catch" muscle has not been found to play a measurable part in effecting motion, yet it has enormous power to maintain posture against great tension. And the exercise of this function is dependent on the innervation of that muscle. The phenomenon is baffling, yet conceivably experimentation, sufficiently refined, would reveal even in the "catch" muscle a release of contractile energy in response to each volley of impulses set up in the appropriate motor nerve. The difference between the "catch" muscle and the contractile muscle might be found to lie in a far more sluggish and far less fatigable response in the former than in the latter, and yet the fundamental nature of the response might be the same in both. Similarly, we might find that the slender muscle fibers innervated by sympathetic nerve fibers in mammalian skeletal muscles, respond to excitation by nerve impulses with measurable contractile effort, but differ from the coarser fibers in the sluggishness of their contraction. If this were the case, and if the slender fibers participated in the general proprioceptive reflexes which Sherrington has demonstrated in the decerebrate mammal, then they would contribute relatively more than the coarse fibers to the plastic or postural property of these reflexes, for the greater duration of each contractile response would serve for adaptation to the sustained effort of maintaining posture. But experiments in which the sympathetic nerves are stimulated should reveal a contractile effort, if this were of sufficient magnitude to play an important rôle in the

18. It is conceivable that some special structure, e. g., the neurofibrils, constitute a conducting path, distinct from the rest of the nerve fiber, and that this evokes a response in a corresponding distinct mechanism, e. g., the sarcoplasm, in the muscle; no evidence exists in support of this view, and it is at best pure speculation. Cobb (footnote 1, p. 528).

19. Bayliss, W. M.: *Principles of General Physiology*, London, 1924, p. 536.

mechanical activity of the muscle; yet all such experiments have failed to show any measurable contraction.²⁰ The slender fibers differ less, histologically, from the coarse fibers in mammalian muscle than do the fibers of the "catch" muscle from those of the contractile muscle in the mollusk; therefore, though in the mollusk we might expect to find so sluggish a contraction in the "catch" muscle that it would be difficult to record, we should hardly expect this difficulty to be insuperable in the case of the slender fibers of the mammalian muscle.

In spite of these objections to the theory that the sympathetic nerves control a plastic element in the tonus of skeletal muscles, and in spite of the preponderance of experimental evidence against the existence of any direct influence of these nerves on skeletal muscle, the fact that Hunter and Royle appear to have shown such an effect in certain animals renders it fitting that a careful examination should be made with reliable quantitative methods. For it may be that although decerebrate rigidity is almost as great after the sympathetic nerves have been cut as before, there is still a slight difference which careful experimentation would reveal. If so, it should be revealed consistently in a large series of animals.

There is one important fallacy in the argument of Hunter and Royle which must be noted. They contend that plastic tonus is maintained by sympathetic nerve fibers, yet they also say that the effect of sectioning these nerves becomes greater for days and even weeks after it is done. Now it has been shown, with a string galvanometer and an electron-tube amplifier connected with a skeletal muscle, that rapid section of the motor nerve evokes functional responses in the muscle for about a minute, after which the muscle becomes wholly inactive;²¹ in other words, the freshly cut surface of the nerve continues to be a source of excitation and to initiate nerve impulses for this length of time and no more. The foregoing is probably the most sensitive known method of detecting functional responses in muscle. It is improbable that nonmedullated nerve fibers differ from medullated fibers profoundly in this respect, and it is safe to conclude that within a few minutes after section, all impulses have ceased to flow to the denervated muscle. Therefore, whatever change in behavior results from stopping the stream of nerve impulses to these muscle fibers, it should be fully established a few minutes after the operation. Further changes, requiring days or weeks to develop, cannot be due to the simple cessation of motor-nerve impulses. If these changes develop they must be due to some secondary cause, such as a shift in circulation or a modification in the physical state of the fibers from disuse. In looking for effects of

20. Cobb (footnote 10). Wastl, H.: *J. Physiol.* **60**:109 (July) 1925.

21. Forbes, A., and Cattell, M.: *Am. J. Physiol.* **70**:140 (Sept.) 1924.

removal of the sympathetic nerve supply, we should therefore seek in the *immediate* result of the operation evidence as to the direct dependence of mechanical effects on sympathetic nerve impulses; and we should also follow the delayed effects of the operation in an effort to see whether indirect or secondary changes could be found corresponding to those described by Hunter and Royle.

These authors maintained that the effects they described appeared better in the goat than in the cat. Their conclusions were based on the most favorable six out of nine or ten experiments on goats, and it seems to us that a much larger series of animals is required to justify conclusions. Aside from the fact that it was not feasible to obtain and handle goats in large enough numbers for an adequate series, we felt that, if there were indeed a physiologic phenomenon of significance for mammals in general and therefore having a bearing on human surgery, it should be possible to demonstrate it in the cat. Furthermore, extensive experience with decerebrate cats over many years furnished a background for comparison, which was lacking in the case of the goat. We have, therefore, used cats in our experiments.

METHOD

In twenty-five cats the sympathetic innervation of either a fore limb or a hind limb was surgically destroyed. Of the twenty-five animals, seventeen were successfully decerebrated and the subsequent condition of all four limbs was carefully examined. Since, for the reasons already given, the loss of any true functional response in a muscle should immediately be apparent, cutting the sympathetic nerves after decerebration should serve to reveal the alleged function, if it really exists. We therefore performed three experiments in which the animal was decerebrated first. The degree of decerebrate rigidity was noted in all four limbs, then the sympathetic innervation of one of them was destroyed and the result of this destruction sought at once. But since the observations of Hunter and Royle suggested the possibility of some delayed secondary effect of interrupting the sympathetic nerve supply, it seemed best to follow their procedure in the majority of our experiments; that is, to do a preliminary aseptic operation in which the sympathetic innervation was destroyed and then, after a suitable interval, to decerebrate the animal and compare the limb in question with the others. Of the seventeen successful experiments, six dealt with the hind limb and eleven with the fore limb. The fore limb seemed preferable for the reason that the entire sympathetic nerve supply of one limb can be destroyed by the rapid operation of removing the stellate ganglion, an operation that has been employed in this laboratory in connection with other researches.²² This operation requires only about fifteen minutes in

22. Cannon, W. B.; Lewis, J. T., and Britton, S. W.: To be published.

the hands of a practiced operator and involves no possibility of disturbing the sympathetic supply of the opposite foreleg. The operation for interrupting the sympathetic innervation of the hind leg involves extirpation of the abdominal sympathetic chain for several segments and is a much more severe and difficult operation. It was done, however, in six cases in order that a certain number of our experiments should duplicate as nearly as possible the procedure of Hunter and Royle.

Experiments of this sort are teeming with possible sources of error, and we therefore devoted particular attention to the appraisal and elimination of these as far as possible. Experience with a great many decerebrate cats has shown us that there are frequently differences in decerebrate rigidity between the two sides of an animal. One possible cause of this might be asymmetrical transection of the brain-stem in decerebrating. With this in mind, we took pains to make the transection as symmetrical as possible.

The influence of the position of the animal as a whole, and in particular of the neck muscles, has been shown by Magnus and De Kleijn²³ to be great in determining the distribution of decerebrate tonus among the muscles of the various limbs. In previous researches, our experience has shown that when a decerebrate animal is left lying on one side, the limbs of the side on which it lies usually exhibit greater rigidity than the opposite limbs. This may be due to some such influence as Magnus has traced to the neck muscles, or it may conceivably result from unequal distribution of the blood supply in the brain-stem or spinal cord, due to the force of gravity. In our experiments, therefore, we took pains to maintain the animal in as perfectly symmetrical a position as possible from the time of decerebration throughout the experiment. This was usually done by placing the animal astride a holder which supported the trunk and allowed the limbs to hang down vertically on the two sides. In order to determine the amount of error that might result from a slight lack of symmetry in position, and also any influence of neck posture, we made a point of rotating the head and neck in various planes—both to right and left—and noted the degree of rigidity in all four limbs with the head held in many different positions.

Another possible source of error to be guarded against is that due to the effect of manipulation of the limbs under observation. The lengthening reaction, described by Sherrington, consists in the relaxation of the extensor muscles when the limb is passively flexed, and appears to result from a reflex inhibition due to proprioceptive impulses. In feeling the resistance of the limb to passive flexion one is apt to induce the lengthening reaction to a greater extent in the limb on which the

23. Magnus, R., and De Kleijn, A.: *Pflüger's Arch. f. d. ges. Physiol.* **145**: 455, 1912.

supply of the knee extensors also was involved in this operation. Great care was exercised to avoid injuring the opposite sympathetic chain.

Decerebration was regularly performed under deep ether anesthesia, with the Sherrington guillotine.²⁴ The carotid arteries were first ligated, and then, while an assistant compressed the vertebral arteries to restrain hemorrhage, a large chisel was driven through the cranium, guided by certain landmarks, in such a way that the transection of the brain-stem occurred at about the level of the anterior colliculi. Usually the first transection with the chisel was practically symmetrical and at approximately the desired level, but to make sure of this point, the brain-stem was quickly examined and any slight lack of symmetry found was corrected with a sharp knife. The symmetry of transection usually was further verified at necropsy. Pressure was continued on the vertebral arteries until clotting stopped further hemorrhage. As soon as the transection was made, the animal was placed astride the holder already mentioned, in order to maintain a strictly symmetrical posture.

Methods of Observation.—In animals sympathectomized before decerebration (constituting all but three of our series) the general condition was watched, and though no measurements were made, observation would reveal any marked lack of symmetry of action. After decerebration, the rigidity was tested manually by placing one hand under each foot and lifting simultaneously. As already mentioned, more decerebrate rigidity is sometimes found on one side than on the other in both fore and hind legs, irrespective of any sympathetic operation. In any given experiment the sympathetic operation involved only one leg, leaving one pair unaffected for use as control. In order to avoid interpreting an inherent difference as evidence of an operative change, we not only compared the operated limb with its mate, but also made a similar comparison between the two limbs of the unaffected pair. For example, when the stellate ganglion was removed we not only tested the fore limbs but the hind limbs as well.

This crude manual method of comparison served very well to reveal any real and consistent differences in rigidity between the two sides; but to render our observations as strictly quantitative as possible, we made use of spring balances. Two somewhat different ends were sought in these measurements: (a) to compare the rigidity in the two legs at the same moment, by a method which should reveal inequalities as surely and accurately as possible, and (b) to obtain an absolute measure (even if only approximate) whereby we could assign a value to the rigidity, making it comparable in a given limb from hour to hour and even in

24. Sherrington, C. S., and Miller, F. R.: *Quart. J. Exper. Physiol.* 9:147, 1915.

corresponding limbs of different animals. The method which proved most satisfactory for the first purpose was to tie spring balances by means of threads to symmetrical points near the feet on the two limbs to be compared, and to pull with both balances in a parallel direction such that the pull tended to flex both limbs. Sometimes we compared the resulting flexion on the two sides, under equal tension, but we found it more satisfactory to pull with tension sufficing to produce symmetry in the position of the two legs, i. e., equal flexion, and then measure the requisite tension on each side. The latter procedure was adopted as our standard method, and was repeated with two or three different degrees of flexion in each comparison.

This method was the most satisfactory for determining whether or not the rigidity was the same or different in a pair of limbs, and by supporting the animal above the table by trunk and hip, to enable the thread to pass the flank without friction, it could be applied fairly well even when the animal lay on one side. But to provide a more absolute measure of rigidity the correlation of angle of flexion with tension was desirable. In order to measure muscle tension in the fore limbs in this way we placed the animal astride the support, tied a string around the elbow on one side, led it round the rear end of the support and tied it to the elbow on the other side. This string was tied tight enough to prevent forward motion of the shoulder joints. A string was then tied to each fore limb at the wrist, care being taken to apply them at exactly symmetrical points, and the hooks of the spring balances were inserted into loops at the ends of these strings. A steady pull with each spring balance at various tensions, perpendicular to the line of the radius, was maintained, and the resulting angles between this bone and the humerus on each side were measured. To facilitate this, we first measured the angle between the humerus and the horizontal string which passed around the back of the support. Since the string held the humerus in a fixed position this angle served as a convenient constant. Thereafter, in the individual measurements, the angle between the radius and the horizontal string was recorded (fig. 1). This was done by holding the straight edge of a celluloid protractor in line with the radius, and reading off the angle thus made with the horizontal string. It was much easier to make accurate measurements in this way than by attempting to measure the angle between the radius and the humerus directly.

In observations on the hind limb the ankle was used as the test joint. Sutures of white thread were passed through the skin, marking the position of the femur from hip to knee and of the tibia from knee to ankle. The knee joint was so held by an assistant that these threads made a right angle, and the two feet were pulled by spring balances tied to them with threads. The bony prominences were used as land-

marks to insure symmetrical application, and the pull was exerted perpendicularly to the metatarsal bones. The angles which these made with the tibia were recorded by means of the celluloid protractor. In this way the decerebrate tonus of the gastrocnemius muscle was measured. The precaution of holding the hip and knee fixed is important, since the position of these joints is a factor in determining the tension on the gastrocnemius muscle. Great pains were taken, therefore, to hold the hip and knee joint rigidly in as symmetrical a position as possible, while the tonus of the gastrocnemius was being measured in this way. This method could be used either with the animal astride the support or lying on one side.

When the animal was astride the support we were able to combine the absolute and relative measures. In the case of both fore limbs and

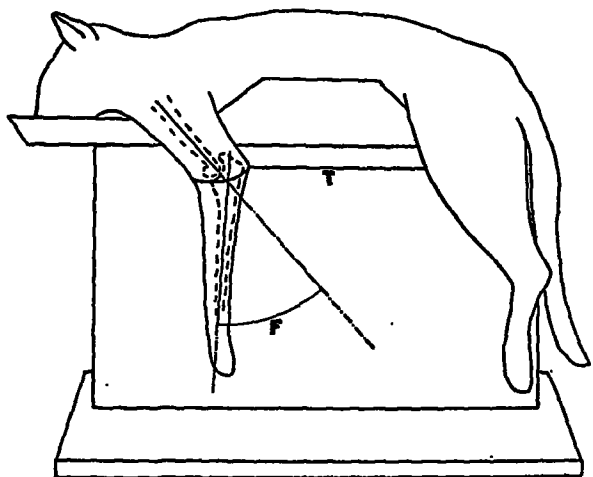


Fig. 1.—Cat astride holder, showing method of measuring angle of elbow flexion: *T*, thread passing from elbow around the rear end of holder *F*, angle of flexion, used in figure 2 and table.

hind limbs we sometimes exerted the same pull on the two sides and measured the angles. In other cases, we pulled the joints to the same angle and compared the tension on the two sides. In making these observations we paid attention to the degree of accuracy attainable and the resulting dependability of the measurements. To this end we often repeated the measurements several times in each case.

In some experiments, electromyograms were made from extensor muscles. This was usually done in the case of the gastrocnemius muscle. Small windows were cut in the skin, one over the middle, the other over the tendinous end of the muscle, and agar electrodes, previously described,²⁵ were applied with sutures through the fascia. These were

25. Forbes, A., and Olmsted, J. M. D.: *Am. J. Physiol.* 73:25 (June) 1925.

Our first experiment was especially favorable for this purpose, since after decerebration (before the sympathetic operation) the cat, when held in a symmetrical posture, showed symmetrical rigidity, as nearly as we could judge by palpation. When the cat was laid on the left side, the rigidity at once became slightly but distinctly greater in the left hind leg than in the right. When placed on the right side, the rigidity was much greater in the right hind leg than in the left. The position was again reversed and again the rigidity became slightly greater in the left leg. Applying the spring balances simultaneously, with pulls sufficing to produce symmetry in the position of the two legs, the tension on each side was measured; this was repeated with two or three different degrees of flexion. The measurements clearly corroborated the findings on palpation, showing the leg on which the animal lay to be the more rigid of the two. For instance, with the cat on the right side, when the rigidity was felt to be much greater in the right leg, the tension required for symmetry was as follows: right, 200 Gm.; left, 90 Gm.; at greater flexion, right, 250 Gm.; left, 110 Gm. When we pulled with equal tension on the two sides, the displacement of the legs, measured in centimeters, harmonized with the foregoing measurements, the more rigid leg showing the less displacement.

To test the source of error arising from the proprioceptive effects described by Magnus and De Kleijn, we rotated the head in this animal and found changes in rigidity, which could be recorded quantitatively by correlation of angle with tension. Raising the head, as the cat lay on one side, caused a measurable loss of rigidity in the uppermost hind leg, the average difference at equal tensions being about 14 degrees of flexion.

After a series of observations of this sort, lasting about two hours from the time of decerebration, the abdominal sympathetic chain was laid bare. Then for another forty minutes similar observations were made, to make sure there was still no marked difference in rigidity between the two hind legs. Then the left sympathetic chain was removed from the crus of the diaphragm approximately to the pelvic brim, thus eliminating all but the last ganglion involved in the innervation of the leg muscles. For a few seconds after this procedure no rigidity could be felt in the left leg. Within a minute it had returned and was for a time greater, by the spring-balance test, than just before removal of the ganglions. More fluctuations followed, but no marked, consistent difference between the two sides. If there was any real diminution of rigidity in the sympathectomized leg, it was too slight to be distinguished from the usual spontaneous fluctuations.

The second animal in which decerebration preceded sympathectomy was also favorable for the desired comparisons. After decerebration the

rigidity was symmetrical in the two sides, as far as palpation could determine, whether the animal was astride the support or lying on one side. A comparative test of angles in the ankle joint with the spring balance, made first on the left leg with the animal on the right side, and then in the reverse arrangement, showed a strikingly close agreement between the two sides. Raising the head caused slight loss of rigidity in the uppermost limb, as in the previous animal. There was some convulsive activity and there were fluctuations of rigidity before the sympathetic operation, which was performed an hour and a half after decerebration. The left abdominal sympathetic chain was removed well into the pelvis. Immediately after the operation there was no rigidity in any of the limbs. In three minutes it returned, and during the next seven minutes both simultaneous palpation and successive spring-balance measurements (the animal first on one side, then the other) clearly and consistently showed *less* tonus on the operated side. This observation would appear to support the findings of Hunter and Royle, but for the fact that at the same time we noted distinctly less rigidity in the left *fore* limb, as well as the hind, although neither fore limb was involved in the operation. We then removed the *right* abdominal sympathetic chain, after which the left hind leg continued consistently to show less rigidity than the right. At this time good myotatic reflexes were shown by electromyograms on the right side, but none on the left. It was also noted that the lengthening and shortening reactions of Sherrington (plastic tonus) were present in the right leg after its sympathetic innervation was removed. Thus this animal proved in the end to afford no support to the theory of sympathetic plasticity, but rather to show how deceptive an experiment of this sort may be, in consequence of uncontrolled changes.

The third animal decerebrated before sympathectomy also showed symmetrical rigidity when placed astride the support, both in the fore and hind limbs. Ten minutes after decerebration the left stellate ganglion was removed. Four minutes after this operation the rigidity was marked in both fore legs, the cat lying on its back. Two observers thought there was a little less rigidity on the operated side; a third observer was unable to detect any real difference by palpation. Five minutes later, with the animal astride the support, no difference at all could be felt between the two sides. When four minutes had elapsed a careful simultaneous test with spring balances showed complete symmetry of rigidity in the fore legs. Angles of elbow flexion correlated with tension, in a long series of tests, showed almost perfect symmetry in the forelegs for the next half hour. There were fluctuations from moment to moment, but when the tests were simultaneous, the hind legs also showed symmetry within the limits of observational error. The

lengthening and shortening reactions of plastic tonus were elicited in both hind legs. In the fore limbs, in which rigidity was greater, it was possible to obtain an imperfect lengthening reaction; that is, the elbow yielded slightly to forced flexion, but release of the foot was followed by full extension. No difference in this respect was found in the two sides. For four hours after excision of the ganglion, no difference could be felt between the two sides. Five and a half hours after operation a slight but definite difference was noted, the operated side showing a little less rigidity. Three hours later there was no perceptible difference, but eleven and a half hours after excision of the ganglion the difference was again definite. No further observations were made.

These three experiments serve to show that fairly wide variations in decerebrate rigidity may result from placing a cat in an unsymmetrical posture. They also show that when the animal is carefully maintained in a perfectly symmetrical posture, rigidity is usually symmetrical, that is, equal in the two limbs of a pair, and thus affords a fair basis for testing the effect of the sympathetic operation. But this symmetry cannot be regularly relied on, for uncontrollable fluctuations occasionally occur in a way that may confuse the effects of an operation.

As to the effect of destroying the sympathetic innervation in these experiments, we should note that in both abdominal operations there was an immediate loss of rigidity, in one case involving all the limbs. This may well have been due to the reflex inhibition of rigidity by the powerful sensory stimulation involved in the operation. If so this phenomenon has no bearing on the problem of sympathetic innervation. The observations made after the requisite time had elapsed for such sensory stimulation to cease showed no definite and consistent effect on rigidity resulting from the operation. The third animal (stellate) showed the most persistent lessening of tonus on the side operated on, but even in this case it was intermittent, with interspersed periods of symmetry, and the difference was too slight to warrant any conclusions.

As was stated in the section on method, in all of our experiments except the three just described, the removal of sympathetic innervation, stellate or abdominal, was performed aseptically first, and then after an interval varying from three to eighty days the animal was decerebrated. In practically all these experiments repeated observations were made with a spring balance, by the methods described above, affording, as far as possible, both the immediate, simultaneous comparison in a given pair of limbs and the more absolute, if rougher, measure wherein the angle of flexion was correlated with tension. A few typical curves illustrating the latter correlation are given for individual experiments. Each curve is made up of measurements taken in rapid succession to avoid confusion due to progressive or fortuitous changes of rigidity. In some cases two

measurements of angle were made at each tension and the measurements averaged. In all cases shown in these curves the animal was astride the holder and both limbs of the pair under observation were pulled symmetrically, the readings being made first from one, then the other. Figure 2 shows four pairs of curves from the fore limbs in the case of three stellate experiments. The method of plotting used by Kuntz and

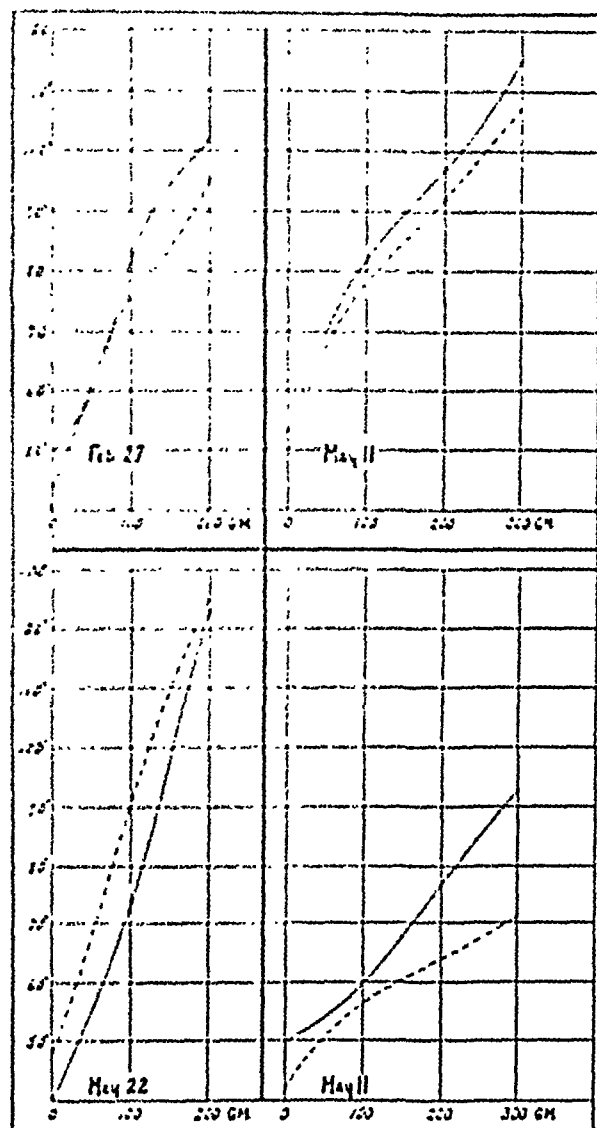


Fig. 2.—Curves correlating elbow flexion with flexing force applied in stellate experiments: abscissae, tension applied to wrist perpendicular to ulna; ordinates, degrees of flexion (described in text); solid line, limb operated on; broken line, control. February 27, three days after operation, measurements made one hour after decerebration; May 11, seventy-six days after operation, upper curves twenty minutes, lower curves three hours after decerebration; May 22, seventy-four days after operation, one and one-half hours after decerebration.

Kerper⁹ is employed, the angles being the degree of flexion of the elbow joint; i. e., its departure from 180 degrees. The curves of February 27 show slightly greater flexion (signifying less rigidity) on the side operated on, especially with the maximum flexing force. The same is shown in both pairs of curves of May 11, especially in the second pair, made an hour and a half after the first. The curves of May 22, on the other hand, show more rigidity in the leg operated on. Figure 3 shows curves from three of the abdominal sympathetic experiments, the angles being the degrees of flexion in the ankle joint. They show slight differences between the two sides, but as in the stellate experiments, the average suggests a slight decrease in rigidity on the

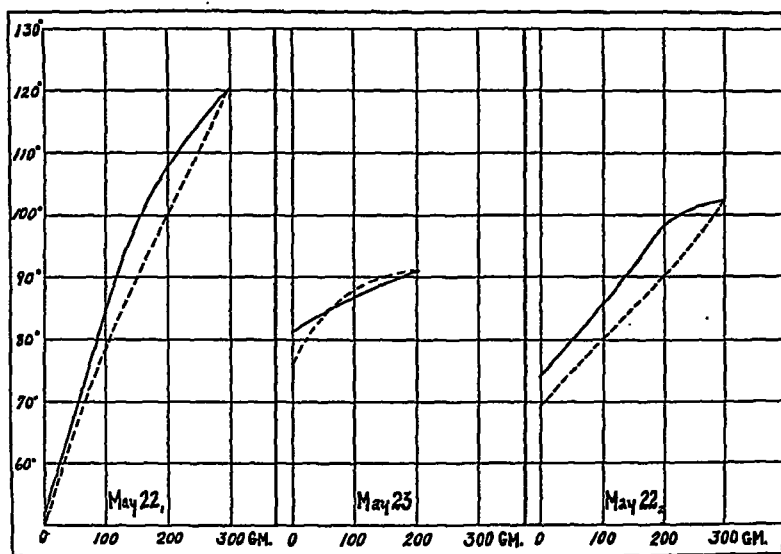


Fig. 3.—Curves correlating ankle flexion with flexing force applied in abdominal sympathetic experiments: abscissae, tension applied to foot perpendicular to metatarsal bones; ordinates, degrees of flexion; solid line, operated limb; broken line, control. May 22, four days after operation, measurements forty minutes after decerebration; May 22, seventy-three days after operation, measurements fifty minutes after decerebration; May 23, sixty-eight days after operation, measurements one hour after decerebration.

side operated on. The differences are usually small, however, compared with the differences appearing between corresponding limbs in different animals or, indeed, between different groups of measurements in the same animal, when a lapse of time has occurred between the measurements.

The results taken as a whole are summarized in the accompanying table. In this table we have included the most complete of the first three experiments, in which decerebration was performed before sympathectomy, and all of the experiments in which these operations were performed in the reverse order. In columns 4-7 are given the

General Summary of Results

| Date of Decere- bration | Type of Operation | Time in Days | Average Angle in Pair Operated On | | | | Average Excess Tension for Equal Flexion, per Cent | Mean Devi- ation | Results of Palpation | | Sum- mary |
|-------------------------------|----------------------|-----------------|-----------------------------------|--------------|-----------------|--------------|---|------------------------|--|---|--------------|
| | | | 100 Gm. Tension | | 200 Gm. Tension | | | | Pair Operated On | Pair Not Operated On | |
| | | | O Degrees | O Degrees | O Degrees | O Degrees | | | | | |
| Feb. 18 1925 | Left stellate | 0 | 35 | 33 | 45 | 42 | .. | .. | Symmetrical; sometimes slightly less | Symmetrical | 0* |
| Feb. 27 | Left stellate | 3 | 82 | 76 | 102 | 95 | 15 | 24 | Symmetrical; slight fluctua- tions | Symmetrical | + |
| March 2 | Left stellate | 6 | 59 | 56 | 66 | 70 | 4 | 12.5 | Symmetrical; varying to more | Symmetrical | - |
| May 15 | Left stellate | 7 | .. | .. | ... | ... | 25 | 25 | Symmetrical | Symmetrical | 0 or + |
| May 18 | Left stellate | 10 | 79 | 68 | 90 | 95 | 13 | 31 | Symmetrical | Symmetrical | 0 or + |
| June 11 | Left stellate | 10 | 97 | 91 | 135 | 123 | 15 | 10 | Symmetrical; sometimes slightly less | Symmetrical | + |
| June 11 | Right stellate | 27 | 69 | 70 | 101 | 127 | 16 | 12 | Symmetrical | Slightly less in right leg | 0 |
| May 23 | Right stellate | 51 | .. | .. | ... | ... | .. | .. | Symmetrical | Symmetrical | 0 |
| May 22 | Left stellate | 71 | 73 | 90 | 123 | 125 | -2 | 15 | Symmetrical; varying to more | Variable | - |
| May 11 | Left stellate | 76 | 71 | 67 | 88 | 78 | 3.5 | 31 | Symmetrical | Variable, sometimes less in left leg | + |
| May 28 | Left stellate | 80 | .. | .. | ... | ... | 100† | .. | Symmetrical; varying to less | Variable; usually symmetrical | 0 or + |
| May 22 | Left abdominal | 4 | 83 | 79 | 108 | 100 | -2 4 | .. | Symmetrical; at one time very slightly more | Symmetrical; with variation | 0 |
| June 12 | Left abdominal | 11 | .. | .. | ... | ... | -33 | 31 | Symmetrical; varying to more | Symmetrical; varying to more in left | - |
| May 23 | Left abdominal | 68 | 89 | 88 | 91 | 91 | 25 | 11 | Less; later approaching symmetry | Symmetrical | + |
| May 22 | Left abdominal | 73 | 85 | 80 | 98 | 90 | 4 | 12 | Symmetrical | Symmetrical | 0 |

* In this experiment the corresponding averages for the pair of limbs not operated on (hind legs) were as follows: for 100 Gm., left 5S degrees, right 45 degrees; for 200 Gm., left 75 degrees, right 47 degrees.

† There was only a single pair of measurements of this type in this experiment. Column 3 shows the interval between sympathectomy and decerebration. Columns 4 to 7 show averages of angles of flexion on the two sides with equal tension. 0 signifies side operated on; C, control. Column 8 gives average percentage of excess tension on the more right side when limbs were pulled to equal flexion; + signifies less tension required on side operated on; - signifies the reverse. Column 9 gives the mean deviation of all measurements from the averages given in column 8. Columns 10 and 11 are condensed results of observation by palpation, for the pairs of limbs operated on and not operated on, respectively. "More" and "less" refer to rigidity in the limb operated on as compared with its mate. Column 12 summarizes results of all methods combined, + signifies definite preponderance in favor of decreased rigidity in limb operated on, - signifies the reverse. 0 signifies symmetry throughout or approximately equal evidence pointing in opposite directions; 0 or +, slight or doubtful preponderance of positive evidence.

averages of measurements of the significant angles. As in the case of figures 2 and 3, the angles express the flexion of elbow or ankle. The range of variation among individual measurements making up these averages was in the neighborhood of 20 degrees.

In column 8, showing comparisons of tensions which induced equal amounts of flexion on the two sides, each number represents the average difference for all measurements made during the course of the experiment. The difference is expressed as the percentage of excess tension on the side on which it was greater. In almost every experiment there were both positive and negative differences in the individual measurements and widely divergent values; the range of variation is indicated in column 9.

The next two columns give the results of comparisons made merely by palpation, i. e., without the spring balance. By comparing the results in columns 4, 5, 6, 7 and 8 with those in column 10 we can form an idea of the amount of agreement between the quantitative measurements and the judgments based on feeling.

The final column summarizes the results of both quantitative measurement and palpation for each experiment. Four experiments gave positive results, that is, supporting Hunter's view; while three were negative, pointing to the opposite conclusion. Eight experiments showed symmetry or at most slight and doubtful positive results, making with the three negative experiments in the table and the two other preliminary experiments not tabulated, a majority of thirteen out of seventeen, which failed to support Hunter's view.

In appraising these results it should be emphasized that we found a strong tendency during supposedly symmetrical palpation to focus the attention on the limb operated on, and in making the comparison to manipulate it more than its mate. As already stated, this manipulation tends to decrease the rigidity in consequence of the lengthening reaction described by Sherrington. It therefore constitutes a highly deceptive source of error which may account for the tendency to detect a lessening of tonus on the side operated on.

It was noted in the introduction that Hunter insisted on plasticity in tonus, revealed by the shortening and lengthening reactions, as the special property lost in consequence of sympathectomy. In most of our experiments the limbs were examined with especial reference to plastic tonus; that is, we noted whether the lengthening and shortening reactions could be evoked and whether the limb operated on differed in this respect from its mate. Our observations showed regularly that these reactions can be evoked in sympathectomized limbs, and in general we found no difference in this respect between the limb operated on and its mate. In two instances there was slightly more plastic tonus on the side operated on.

The animal decerebrated May 23, sixty-eight days after abdominal operation, showed the largest and most consistent difference of the sort found by Hunter. We therefore saved specimens of the extensor muscles under observation on the two sides and had them sectioned and stained with hematoxylin and eosin. Dr. Stanley Cobb examined these sections and reported both specimens normal and indistinguishable, as far as he was able to observe, under the microscope.

The animal decerebrated March 2, six days after the stellate operation, is an example of the fortuitous changes of rigidity which render difficult a strict quantitative treatment of this problem. This animal for



Fig. 4.—Appearance of animal two hours after decerebration, six days after left stellate operation, showing persistent maintenance of *greater rigidity* in limb on which operation has been performed.

a time showed symmetrical rigidity on the two sides. About an hour after decerebration a marked and persistent increase in rigidity appeared on the side operated on as compared with the control. The animal was placed on its back, whereon the limb operated on persistently retained its posture of extension against gravity, while the limb not operated on dropped into a flexed position in the manner described by Hunter as typical for the limb operated on. This paradoxical condition lasted for more than an hour, during which time the photograph shown in figure 4 was taken. The picture would be quite typical of the condition described by Hunter and Royle, but for the fact that in this case it was the limb operated on, and not the control, whose rigidity maintained the extended

posture against gravity. The characteristic change in the nictitating membrane eliminated the possibility of any error as to which was the operated side.

On the whole our results show a slight preponderance of readings which indicate less rigidity on the side operated on. A careful examination of the table, however, shows that the differences between the two sides are usually small compared with the differences between the absolute measurements in the series of experiments. And it should be emphasized that most of the figures in the table are averages made up of individual figures showing fairly wide variation. In other words, if there is any loss of rigidity traceable to sympathectomy it is small compared with the fluctuations due to other causes. Since the majority of our observations show almost perfect symmetry of rigidity after, as well as before, sympathectomy, and since observations showing actually greater rigidity on the side operated on are not uncommon, it is fair to conclude that if sympathectomy has any effect at all on decerebrate rigidity it is at most insignificant. We cannot positively exclude such an effect; neither can we conclude that our data, or indeed any other with which we are acquainted, suffice to indicate its existence.

Recalling that Hunter emphasized the need of waiting days or even weeks after sympathectomy before decerebrating, let us turn to the table to see whether there was any tendency for the effect he described to increase as the interval increased. The observations are arranged in the order of the number of days elapsing between sympathectomy and decerebration, first in the case of the stellate and then of the abdominal operations. No such correlation appears, and we are therefore unable to verify the existence of any delayed effect such as has been alleged.

In three of the animals decerebrated after unilateral sympathectomy we compared the electromyograms of the extensor muscles in the limb operated on and in its mate. Records were made of rigidity, undisturbed by applied tension, and of the myotatic responses to forced flexion, equal tensions being applied to the two sides in alternation. On the intact side there was no clear evidence of tonus without action currents; that is, the apparent amplitude of the action currents in general corresponded with the tension which the rigidity was resisting. Furthermore, no regular difference in this respect was found between the two sides.

COMMENT

Our evidence, as well as the theoretic considerations outlined in the introduction, lead us to substantially the same view that has been set forth by Walshe.²⁶ Perhaps the strongest reason for supposing that the sympathetic nerves play a significant rôle in maintaining tonus in skeletal

26. Walshe, F. M. R.: *Med. Science* 12:437 (Sept.) 1925.

muscle is the histologic evidence for the existence of certain muscle fibers innervated by these. It is perhaps premature to accept these anatomic findings as conclusively established for limb muscles, but they seem to have been supported by degeneration experiments in the hands of such competent workers that their validity is probable in the muscles that have been examined. If an appreciable number of skeletal muscle fibers in the limbs are innervated in this way, it is hard to conceive of such a neuromuscular mechanism existing without functional significance. Sympathetic innervation in itself suggests the possibility of a relatively sluggish type of contraction. Moreover, several workers²⁷ have shown that the red fibers respond more sluggishly than the white, both as regards their action currents and their contraction. The postulation of a catch mechanism for plastic tonus, distinct from the contractile mechanism, is a natural consequence of the superficial resemblance between plastic tonus and the behavior of the molluscan adductor. Needham¹⁶ suggests that the red fibers may possess a catch mechanism for tonus and a separate contractile mechanism for shortening, whereas the white fibers possess only the contractile mechanism. How can we reconcile such mechanisms with the fact that a nerve when excited responds with only one kind of impulse, and the regular consequence of this is a contractile response in the innervated muscle—a response that cannot be graded in quality or quantity except so far as the frequency of excitation or the load encountered is altered? A catch mechanism in the red fibers, distinct from their contractile mechanism, would require either a separate neural path or a property in the muscle of responding in a special way to a limited range of frequencies in the nerve impulses. An obstacle to assigning the alleged sympathetic function to the red fibers is the observation of Hay²⁸ that they are innervated by medullated nerve fibers. A much simpler view than that of dual function would be that each muscle fiber, whether red or white, slender or coarse, has only one type of functional response, but that such fibers as have sympathetic connections contract more sluggishly than those innervated directly from the spinal cord. On this view we should expect the muscle as a whole to contract and relax more briskly after sympathectomy, since the quicker white fibers are still in action and the slower fibers have ceased to function. If then we regard tonus simply as a nicely balanced and sustained series of proprioceptive reflexes, as Cobb contends, then throwing the more sluggish fibers out of action should render tonus less plastic. If the limb muscles really possessed the alleged sympathetic innervation, it is quite possible that this would be the case, but our results show that the change, if it occurs at all, is insignificant. This conclusion is rein-

27. Cobb (footnote 1, p. 520).

28. Hay, J.: *Liverpool M. & Chir. J.* 21:431, 1901.

forced by the recent evidence of Huggett and Mellanby²⁹ on the absence of influence on tonus of those drugs affecting autonomic endings.

Hunter contended that the effect of sympathectomy on tonus becomes progressively greater for many days after the operation. We would again emphasize that such a progressive change, if established, would prove that the loss of tone was not directly due to the cessation of motor-nerve impulses, since these impulses must cease to flow immediately after section of the nerve. The effect would necessarily depend on secondary causes. If the loss of tone really occurred, it might conceivably result because disuse would render the fibers softer and more extensible and therefore less prone to resist deformation of the muscle as a whole, or it might be due to circulatory changes. On reference to the accompanying table it will be seen that the two most definitely positive experiments in our series were on animals decerebrated three and ten days after sympathectomy. On the other hand, we find two negative experiments at six and eleven days, and two symmetrical experiments at four and seven days. These observations point to the view that we are dealing rather with haphazard or chance fluctuations than with any definite results of the operation. Certainly no tendency to a progressive increase in the loss of tonus appears in our table.

Physicians and surgeons who have observed cases of spasticity in which ramisection was performed have described them to us. In one case, at least, careful observation before and after operation showed no relief from the spastic condition. In two cases, on the other hand, the operation seemed to produce some degree of temporary and even permanent improvement. Such cases and those reported by Royle, together with the apparently positive experiments on goats, appear to be the chief facts in favor of Hunter's view. How are we to reconcile them with the apparent lack of physiologic basis in our experiments and in those of the majority of other workers? Of our experiments those which seemed to show definite results of the sort described by Hunter and Royle were few. The positive results of others and the surgical successes have also been few. In view of the many possible sources of error in the interpretation of results, and especially in consideration of other possible causes of improvement in the surgical cases—such as exercises, mental suggestion and extra good care—it is perhaps reasonable to conclude that the surgical successes are not much more significant than the small percentage of apparently positive experiments in our series. Looking over the sum total of results from both surgical operations and physiologic experiments reported by a considerable number of workers, we are led to believe that the alleged effects of sympathectomy,

29. Huggett, A. St. G., and Mellanby, J.: *J. Physiol.* 60:8, 1925.

when present, are due to extraneous circumstances and uncontrolled causes rather than to the direct effects of removing the sympathetic innervation.³⁰

SUMMARY

1. Certain investigators have contended that "contractile" and "plastic" tonus in skeletal muscle are two distinct functions, depending respectively on the cerebrospinal, medullated nerve fibers and on those arising from the sympathetic chain. This theory we find to be without adequate experimental foundation, and, in its extreme form, inconsistent with the known facts of nerve-muscle physiology.

2. In a series of cats we have cut the sympathetic innervation of one limb, either immediately after or at intervals varying from three to eighty days before decerebration. In these animals we have compared the decerebrate rigidity of the limb involved in the operation with that of the other limbs, measuring with spring balances the tension required to force various degrees of flexion, and noting the "plastic" features of rigidity.

3. The results have shown wide variations in rigidity, depending on postures imposed on the animal, and almost as great variations apparently dependent on conditions of the experiment not subject to control. Comparison of the operated limb with its mate usually shows almost perfect symmetry, i. e., no appreciable difference. Sometimes there is less rigidity on the side operated on, sometimes more. Averaging the measurements of the entire series showed slightly less rigidity on the side operated on; but this difference was small compared with the individual fluctuations in both directions making up the average.

4. We conclude that if there is any loss of tonus in consequence of the operation it is insignificant. Certainly decerebrate rigidity persists.

30. Since this article was written, an article by S. W. Ranson (*J. Comp. Neurol.* **40**:1 [Feb.] 1926) has appeared in which a lessening of decerebrate tonus, following application of nicotine to spinal ganglions, is cited in support of the theory of plastic and contractile tonus. This article contains no proof of a qualitative change in tonus, and the results might be explained in other ways not involving the assumption of two types of tonus. Another recent paper by Kuntz and Kerper (*Am. J. Physiol.* **76**:121, 1926) ends to support the conception of a plastic function mediated by the sympathetic nerves. Their results are complicated by the presence of the intact cerebrum. A possible explanation may lie in L. A. Orbeli's observation (*J. Petrograd M. Inst.* **6**:8, 1923) which suggests a chemical effect of sympathetic nerve impulses counteracting fatigue and thus aiding sustained contraction under conditions tending to produce fatigue. Still another paper by F. D. Coman (*Bull. Johns Hopkins Hosp.* **38**:163 [March] 1926), which has appeared since our article was written, furnishes three lines of evidence against the view that postural tonus of skeletal muscle is developed or maintained by sympathetic nerves.

at least approximately undiminished, and manifests its plastic features after sympathectomy.

5. This conclusion removes the alleged physiologic basis for the surgical operation of ramisection as a cure for spasticity. If patients are in reality improved in consequence of this operation, it is probably due to some incidental feature of their treatment, and not to the interruption of nerve impulses arising in the sympathetic nervous system.

THYROID DISTURBANCES

CLINICOPATHOLOGIC STUDY OF THREE HUNDRED INSTANCES *

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The study of thyroid disease has progressed in a manner similar to that of kidney disturbances. Each has resulted in the introduction into the literature of many classifications. For this reason antagonistic views have always existed between clinicians and pathologists concerning the study of irregularities in these organs.

While, therefore, the literature of the thyroid gland is considerable, comprehensive clinicopathologic analyses that might mitigate these differences have not been found. Most pathologic studies of the thyroid gland have been either in the form of simple academic outlines of pure pathology or as histopathologic studies correlated with certain of the more striking symptoms. One of the earliest classifications of thyroid changes in relation to symptoms was that proposed in 1908 by Wilson,¹ who found that general changes in the thyroid parenchyma paralleled the character and intensity of symptoms produced. Later Wilson² differentiated the pathologic changes in simple and exophthalmic goiters, subdividing the former group into diffuse and nodular types. Shepherd and Duval,³ writing in 1909, reported histopathologic changes found in a series of fifty-nine cases, but concluded that no cytologic changes could be regarded as specific for any special type of disease of the thyroid gland. Following this Marine and Lenhart⁴ introduced a classification based on the principles of pure pathology. While the details are accurate it is perhaps too academic for clinical application. Similarly, McCarty⁵ in 1912 published an elementary analysis of histologic findings in a large number of cases, but without any conclusions as to their significance or possible application. About 1919, Plummer⁶ pointed out that hyperthyroidism could be divided into two separate and distinct types each due to a different pathologic change in

*From the departments of pathology and surgery of the University of Oregon Medical School.

1. Wilson, L. B.: *Am. J. M. Sc.*, December, 1908.

2. Wilson, L. B.: *Surg., Gynec. & Obst.*, June, 1908, pp. 558-602; *Am. J. M. Sc.* **146**:781-790, 1913.

3. Shepherd and Duval: *Tr. Am. S. A.* **27**:56, 1909.

4. Marine and Lenhart: *Arch. Int. Med.* **7**:506-535, 1911.

5. McCarty, Y. C.: *New York State J. Med.* **12**:595, 1912.

6. Plummer, H. S.: *Am. J. M. Sc.* **146**:790, 1913.

the thyroid gland; namely, diffuse hypertrophy and hyperplasia, and adenoma. A later clinical classification by Williams⁷ differentiated simple and toxic goiter. In the same year, Else⁸ introduced a more comprehensive classification, segregating a cardiovascular group. In 1922 Goetsch⁹ introduced a conception of excessive interstitial hyperplasia which he designed adenomatosis, pointing to it as a factor in mild hyperthyroidism. That these changes are not compensatory or regenerative rather than primarily toxic has never been established. Holst¹⁰ in 1923 offered a simple classification based on gross findings. He agreed with Hellwig,¹¹ who had traced the steps of development from simple colloid goiter to a typical exophthalmic gland, that all cases of hypersecretion are conditions of hyperthyroidism and not dysthyroidism. Biedl¹² in 1924 summarized the European conception of thyroid disturbance as follows: (1) simple diffuse struma; (2) simple nodular adenoma, and (3) parenchymatous hyperplastic thyroid. He maintained that true Basedow's disease is seen only in subjects with status thymicolymphaticus. More recently Williamson and Pearse¹³ have introduced a classification based on their conception of thyroid structure. It would seem that detailed observations have been ascribed an unestablished importance in their outline.

Much of the divergence in views held is undoubtedly due to the incomplete knowledge of the structure and physiology of the thyroid gland. In spite of the splendid work of Bensley¹⁴ on the opossum in which he pointed out the mode of secretion, transcellular or intercellular migration, and colloid storage, much remains obscure as to the manner in which the gland responds to stimuli. There is a question as to whether the whole gland may become active in a diffuse way or in a patchy focal reaction. The relative stability of the hormone containing colloid also is unsolved. It is conceivable that an older colloid may hold the active principle with greater tenacity than that more recently formed and stored. The resistance of such colloid stability to demanding stimuli may lead to more responsive portions yielding an overproduction. Then, too, there remains for determination the secretory power of thyroid epithelium as affected by such colloid storage, since the latter in itself may possibly lead to cell atrophy and atony. Williamson and Pearse¹⁵ in their recent

7. Williams, C.: *Am. J. M. Sc.* **161**:223 (Feb.) 1921.

8. Else, J. E.: *Northwest Med.* **20**:118 (May) 1921.

9. Goetsch, E.: *Endocrinology* **6**:59-72 (June) 1922.

10. Holst, J.: *Acta chir. Scandinav.* **4**:1-91, 1923.

11. Hellwig, A.: *Deutsch. med. Wchnschr.* **48**:420, 1922.

12. Biedl, A.: *Ann. Clin. Med.* **3**:444 (Dec.) 1924.

13. Williamson and Pearse: *J. Path. & Bacteriol.* **28**:361-389 (April) 1925.

14. Bensley: *Am. J. Anat.* **19**:37 (Jan.) 1916.

15. Williamson and Pearse: *J. Path. & Bacteriol.* **26**:459, 1923.

work on the structure of the thyroid have offered some interesting data as to the nature of the tubuli, the vascular relationship and the manner in which the solid tubuli develop colloid containing alveoli. It is their opinion that the active agent is delivered into lymph channels. This is in disagreement with others who regard the veins as being the chief carrying channels of the hormone. The question as to whether the thyroid gland can produce anything but a specific hormone in normal, deficient or excessive amounts has never been fully answered.

Although there have been conflicting interpretations of the thyroid in health and disease, there are outstanding facts of common observation. It is generally agreed that the gland varies markedly in size and shape and that clinically it ranges in symptomatology from cretinism and myxedema to hypersecretion or perversion of function as the case may be. In our experience we have been able to group the surgically removed portions, or entire glands, according to their gross characteristics and salient, predominating microscopic pathologic condition as follows:

PATHOLOGIC CLASSIFICATION NORMAL OR ENLARGED GLAND WITH
OR WITHOUT INCREASED OR DECREASED ACTIVITY

I. Diffuse parenchymatous hyperplasia.

1. Gross examination: Compact, ischemic, grayish white and colloid free.
2. Microscopic examination:
 - a. Hyperplasia and hypertrophy of epithelium.
 - b. Peripheral or general vacuolization of colloid.
 - c. Dilatation of lymph channels and engorgement of blood vessels.
 - d. Variable increase in the supporting stroma with or without round cell infiltration.

II. Diffuse adenomatous hyperplasia.

1. Gross examination: Diffuse reddish brown gland without noticeable nodularity or accentuation of lobular markings; variable amount of colloid.
2. Microscopic examination:
 - a. Focal changes similar to Group I.
 - b. Normal or colloid stretched alveoli.
 - c. Focal hyperplasia and hypertrophy of epithelium.
 - d. Inter-alveolar hillocks or intra-alveolar papillomatous projections.
 - e. Focal round cell collections of pseudolymph nodes.
 - f. Focal increased vascularity and dilated lymph channels.

III. Nodular adenomatous hyperplasia.

1. Gross examination: Variable nodular accentuation of the lobular markings with or without excessive colloid storage, cystic degeneration, hemorrhage, scarring or lime salt deposit. The color usually varied with the regressive changes.

2. Microscopic examination:

- a. Focal cytologic changes similar to these found in Groups I and II; compensatory.
- b. Characteristic retrogressive changes.
- c. Areas of adenomatosis.

IV. Solitary adenoma.

1. Gross examination: Variable in size; circumscribed; solitary or multiple; grayish white to dark reddish brown; solid, cystic or colloid filled. Regressive changes may be present.
2. Microscopic examination:
 - a. All stages of fetal types of alveoli.
 - b. Peripheral pseudocapsule formation with round celled infiltration and compressed alveoli.
 - c. Focal neighboring hyperactive areas in adjoining parenchyma.
 - d. Neighboring areas of adenomatosis.

V. Neoplasms.

VI. Inflammations.

1. Pyogenic.
2. Infectious granuloma.

While the gross divisions of the portions of the thyroid removed are rather easily affected according to the foregoing outline, there are numerous instances of the shading of one group into the other. Such glands of border-like nature must be relegated to the group according to the dominancy of certain classifying characteristics. More detailed separations are as futile here as they are in kidney disease.

In the microscopic analysis it is important to establish histologic criteria of activity or rest. We are certain of one thing, namely, that the histologic appearance of the gland in Group 1, diffuse parenchymatous hyperplasia—so-called exophthalmic goiter (Fig. 1)—is just as definite as are the gross and clinical manifestations. This is conceded to be an entity in all respects. We may therefore safely assume that the microscopic pattern found here is one resulting from the production and the delivery of thyroid hormone or its by-products into the lymphatics or veins. There is evidence to show that cellular hypertrophy and hyperplasia, peripheral vacuolization of colloid, dilated lymph channels and veins and the resulting alveolar distortion occur in the order named, and are natural steps in the mechanism of function of any ductless gland and are accompanied by an increased blood supply to the part. Prolonged activity probably leads to the necessity for more supportive stroma and the appearance of special inflammatory absorption reactions consisting of lymph cell collections or pseudolymph nodes (Fig. 2). Finally destruction with areas of adenomatosis (Fig. 3)—probably reconstruction—or a gradual reversal of the process occurs. When the latter is viewed a double row of cells lining alveoli, small papillomatous projec-

tions into large colloid filled alveoli and interalveolar hillocks may be seen (Figs. 4 and 5). The disturbance finally becomes patchy. With such histologic criteria as these in mind one can analyze the thyroids of various groups and gage their relative activity in surprising agreement with the clinical manifestations. One can say with a fair degree of accuracy as to whether a given gland has produced no, slight, moderate, marked, or extreme symptoms.

In view of the foregoing observations it would seem to us that thyroid activity is generally spotty. Excessive colloid storage, nodular modifica-

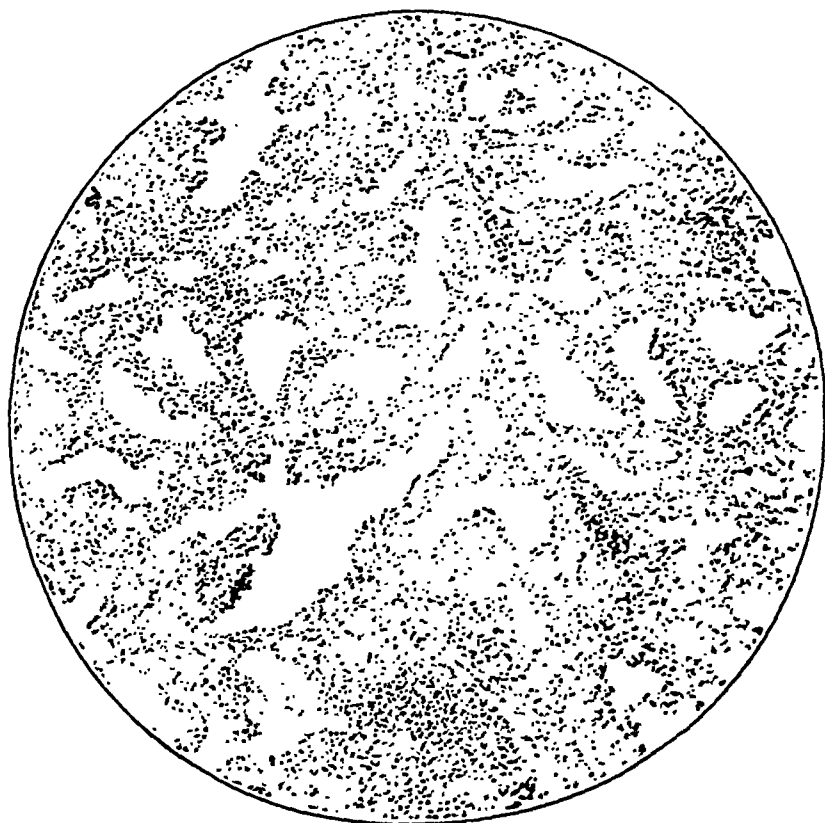


Fig. 1.—Appearance of structural design in the diffuse parenchymatous hyperplasia, so-called exophthalmic goiter.

tion of structure, inflammatory atrophies, and neoplasm in one part may reflect an increased necessity for activity in another or adjacent portion.

With these pathologic conditions in mind we deemed it of sufficient merit to analyze 300 instances of thyroid disturbances in the light of the available clinical data in each case (accompanying table).

COMMENT ON TABLE

It will be seen that thirty-eight of these, or 12.6 per cent., fall in Group 1 (diffuse parenchymatous hyperplasia), 108, or 35 per cent., in Group 2 (diffuse adenomatous hyperplasia), 102 in group 3 (nodular

Composite Clinical Data in Three Hundred Cases

| Pathologic Grouping and Comparison of Composite Cases | | | | | | | | | | | | | | | | | | | | | |
|--|-----|---------------------|-----------|-----|---------------------|-----------|-----|-------------------------|-----------|---------|---------------------|-----------|---------|---------------------|-----------|---------|------------------------|-----------|----------|-----|--|
| Pathologic Grouping—Normal or Enlarged Thyroid With or Without Increased or Decreased Activity | | | | | | | | | | Group 4 | | | Group 5 | | | Group 6 | | | | | |
| Clinical Data | No. | Group 1 | | | Group 2 | | | Group 3 | | | Solitary Adenomas | Per Cent. | No. | Neoplasms | Per Cent. | No. | Inflammatory Processes | Per Cent. | | | |
| | | Diffuse Hyperplasia | Per Cent. | No. | Diffuse Hyperplasia | Per Cent. | No. | Adenomatous Hyperplasia | Per Cent. | No. | | | | | | | | | Adenomas | No. | |
| Total cases.... | 38 | 108 | 12.6 | | 36 | 102 | | 34 | | 41 | | 13.6 | 7 | | 2.3 | 4 | | 1.3 | | | |
| Age..... | | | | | | | | | | | | | | | | | | | | | |
| | 1 | From 0 to 20 yrs. | 3 | 29 | From 0 to 20 yrs. | 3 | 3 | From 0 to 20 yrs. | 3 | 1 | From 0 to 20 yrs. | 3 | 0 | From 0 to 20 yrs. | 3 | 1 | From 0 to 20 yrs. | 25 | | | |
| | 9 | From 20 to 30 yrs. | 23 | 30 | From 20 to 30 yrs. | 27 | 26 | From 20 to 30 yrs. | 10 | 7 | From 20 to 30 yrs. | 18 | 1 | From 20 to 30 yrs. | 14 | 0 | From 20 to 30 yrs. | 0 | | | |
| | 12 | From 30 to 40 yrs. | 31 | 25 | From 30 to 40 yrs. | 23 | 29 | From 30 to 40 yrs. | 26 | 10 | From 30 to 40 yrs. | 26 | 2 | From 30 to 40 yrs. | 26 | 1 | From 30 to 40 yrs. | 25 | | | |
| | 12 | From 40 to 50 yrs. | 31 | 13 | From 40 to 50 yrs. | 12 | 20 | From 40 to 50 yrs. | 29 | 13 | From 40 to 50 yrs. | 34 | 3 | From 40 to 50 yrs. | 34 | 1 | From 40 to 50 yrs. | 25 | | | |
| | 3 | From 50 to 60 yrs. | 9 | 7 | From 50 to 60 yrs. | 12 | 6 | From 50 to 60 yrs. | 10 | 4 | From 50 to 60 yrs. | 16 | 0 | From 50 to 60 yrs. | 0 | 0 | From 50 to 60 yrs. | 0 | | | |
| | 1 | From 60 to 70 yrs. | 3 | 86 | From 60 to 70 yrs. | 80 | 20 | From 60 to 70 yrs. | 91 | 36 | From 60 to 70 yrs. | 10 | 4 | From 60 to 70 yrs. | 10 | 4 | From 60 to 70 yrs. | 50 | | | |
| Sex..... | | | | | | | | | | | | | | | | | | | | | |
| | 29 | Females..... | 80 | 22 | Females..... | 20 | 91 | Females..... | 91 | 5 | Females..... | 11 | 5 | Females..... | 11 | 5 | Females..... | 50 | | | |
| | 9 | Males..... | 20 | 86 | Males..... | 88 | 12 | Males..... | 82 | 35 | Males..... | 85 | 7 | Males..... | 85 | 1 | Males..... | 100 | | | |
| Location..... | | | | | | | | | | | | | | | | | | | | | |
| | 26 | Oregon..... | 68 | 10 | Washington..... | 12 | 82 | Oregon..... | 82 | 35 | Oregon..... | 85 | 3 | Oregon..... | 85 | 5 | Oregon..... | 50 | | | |
| | 10 | Washington..... | 26 | 18 | Unknown..... | .. | 11 | Idaho..... | 11 | 2 | Idaho..... | 2 | 2 | Colorado..... | 2 | 1 | British Columbia..... | 50 | | | |
| | 1 | Idaho..... | .. | 24 | Unknown..... | .. | 3 | Montana..... | 3 | 22 | Unknown..... | 47 | 4 | Unknown..... | 47 | 4 | Unknown..... | 50 | | | |
| | 1 | Utah..... | .. | 47 | Unknown..... | 22 | 38 | Adolescent..... | 54 | 12 | Gradual..... | 54 | 6 | Adolescent..... | 54 | 1 | Adolescent..... | 50 | | | |
| Rate of development | | | | | | | | | | | | | | | | | | | | | |
| | 17 | Unknown..... | 47 | 22 | Unknown..... | 58 | 41 | Unknown..... | 58 | 22 | Unknown..... | 80 | 20 | Unknown..... | 80 | 3 | Married..... | 50 | | | |
| | 8 | Gradual..... | 18 | 42 | Adolescent..... | 12 | 50 | Adolescent..... | 54 | 1 | Fast..... | 54 | 1 | Fast..... | 54 | 3 | Married..... | 75 | | | |
| | 7 | Adolescent..... | 13 | 10 | Fast..... | 12 | 81 | Married..... | 19 | 81 | Married..... | 54 | 40 | From 1 to 6..... | 54 | 3 | From 1 to 6..... | 100 | | | |
| | 6 | Fast..... | 80 | 22 | Single..... | 20 | 19 | Single..... | 48 | 54 | From 1 to 6..... | 40 | 34 | None..... | 40 | 4 | None..... | 50 | | | |
| Marital state.. | | | | | | | | | | | | | | | | | | | | | |
| | 29 | Married..... | 20 | 39 | From 1 to 5..... | 37 | 63 | From 1 to 5..... | 13 | 8 | Of 23..... | 34 | 1 | Of 3..... | 33 | 1 | Of 1..... | 50 | | | |
| | 15 | Single..... | 61 | 68 | None..... | 63 | 48 | None..... | 48 | 23 | None..... | 18 | 8 | None..... | 33 | 2 | None..... | 50 | | | |
| Pregnancies.... | | | | | | | | | | | | | | | | | | | | | |
| | 23 | None..... | 40 | 13 | Of 40..... | 32 | 7 | Of 54..... | 14 | 10 | Influenza..... | 24 | 2 | Influenza..... | 28 | 2 | Influenza..... | 50 | | | |
| | 6 | Of 15..... | 25 | 35 | Influenza..... | 65 | 14 | Influenza..... | 43 | 17 | Measles..... | 72 | 5 | Measles..... | 72 | 2 | Measles..... | 50 | | | |
| Miscellaneous... | | | | | | | | | | | | | | | | | | | | | |
| | 56 | Measles..... | 47 | 50 | Measles..... | 46 | 27 | Measles..... | 27 | 8 | Mumps..... | 19 | 6 | Mumps..... | 84 | 14 | Mumps..... | 25 | | | |
| Previous conditions | | | | | | | | | | | | | | | | | | | | | |
| | 16 | Mumps..... | 7 | 13 | Mumps..... | 12 | 15 | Mumps..... | 15 | 4 | Typhoid..... | 30 | 2 | Typhoid..... | 28 | 0 | Typhoid..... | 50 | | | |
| | 8 | Typhoid..... | 21 | 6 | Tonsillitis..... | 6 | 27 | Tonsillitis..... | 2 | 5 | Scarlet fever..... | 12 | 7 | Scarlet fever..... | 17 | 2 | Scarlet fever..... | 25 | | | |
| | 8 | Tonsillitis..... | 5 | 30 | Whooping cough..... | 8 | 2 | Whooping cough..... | 2 | 7 | Whooping cough..... | 5 | 2 | Whooping cough..... | 17 | 0 | Whooping cough..... | 25 | | | |
| | 31 | Scarlet fever..... | 15 | 12 | Whooping cough..... | 7 | 2 | Whooping cough..... | 2 | 7 | Whooping cough..... | 17 | 2 | Whooping cough..... | 17 | 0 | Whooping cough..... | 25 | | | |
| | 12 | Whooping cough..... | 14 | 2 | Smallpox..... | 7 | 2 | Smallpox..... | 2 | 8 | Smallpox..... | 2 | 2 | Smallpox..... | 2 | 0 | Smallpox..... | 25 | | | |
| | 5 | Smallpox..... | 5 | 13 | Pneumonia..... | 7 | 2 | Pneumonia..... | 2 | 8 | Pneumonia..... | 2 | 2 | Pneumonia..... | 2 | 0 | Pneumonia..... | 25 | | | |

| | | | | | | | | | | | | | | | | |
|-------------------------|----|---------------------------|----|----|---------------------------|----|---------------------------|----|---------------------------|----|----|---------------------------|-----|---|---------------------------|-----|
| Systolic blood pressure | 9 | Unknown..... | 26 | 27 | Unknown..... | 32 | Unknown..... | 32 | Unknown..... | 37 | 1 | Unknown..... | 14 | 1 | Unknown..... | 25 |
| | 2 | From 100 to 120.... | 5 | 20 | From 100 to 120.... | 14 | From 100 to 120.... | 20 | From 100 to 120.... | 27 | 1 | From 100 to 120.... | 17 | 0 | From 100 to 120.... | 0 |
| | 6 | From 120 to 130.... | 15 | 19 | From 120 to 130.... | 22 | From 120 to 130.... | 13 | From 120 to 130.... | 23 | 0 | From 120 to 130.... | 0 | 1 | From 120 to 130.... | 25 |
| | 4 | From 130 to 140.... | 10 | 18 | From 130 to 140.... | 21 | From 130 to 140.... | 14 | From 130 to 140.... | 27 | 1 | From 130 to 140.... | 17 | 0 | From 130 to 140.... | 0 |
| | 7 | From 140 to 150.... | 18 | 15 | From 140 to 150.... | 14 | From 140 to 150.... | 14 | From 140 to 150.... | 27 | 1 | From 140 to 150.... | 17 | 0 | From 140 to 150.... | 0 |
| | 2 | From 150 to 160.... | 5 | 10 | From 150 to 160.... | 8 | From 150 to 160.... | 16 | From 150 to 160.... | 7 | 0 | From 150 to 160.... | 0 | 0 | From 150 to 160.... | 0 |
| | 8 | From 160 to 180.... | 21 | 10 | From 160 to 180.... | 9 | From 160 to 180.... | 23 | From 160 to 180.... | 7 | 3 | From 160 to 180.... | 50 | 2 | From 160 to 180.... | 50 |
| | 9 | Unknown..... | 25 | 27 | Unknown..... | 25 | Unknown..... | 32 | Unknown..... | 37 | 1 | Unknown..... | 14 | 1 | Unknown..... | 25 |
| Pulse pressure | 29 | Known..... | 74 | 81 | Known..... | 75 | Known..... | 72 | Known..... | 63 | 6 | Known..... | 86 | 3 | Known..... | 75 |
| | 0 | From 30 to 40..... | 0 | 3 | From 30 to 40..... | 4 | From 30 to 40..... | 12 | From 30 to 40..... | 15 | 0 | From 30 to 40..... | 0 | 0 | From 30 to 40..... | 0 |
| | 3 | From 40 to 50..... | 10 | 13 | From 40 to 50..... | 4 | From 40 to 50..... | 17 | From 40 to 50..... | 11 | 0 | From 40 to 50..... | 0 | 0 | From 40 to 50..... | 0 |
| | 1 | From 50 to 60..... | 14 | 13 | From 50 to 60..... | 16 | From 50 to 60..... | 18 | From 50 to 60..... | 42 | 3 | From 50 to 60..... | 50 | 1 | From 50 to 60..... | 33 |
| | 7 | From 60 to 70..... | 24 | 29 | From 60 to 70..... | 36 | From 60 to 70..... | 20 | From 60 to 70..... | 11 | 0 | From 60 to 70..... | 0 | 1 | From 60 to 70..... | 33 |
| | 4 | From 70 to 80..... | 15 | 15 | From 70 to 80..... | 18 | From 70 to 80..... | 14 | From 70 to 80..... | 10 | 1 | From 70 to 80..... | 17 | 0 | From 70 to 80..... | 0 |
| | 11 | From 80 to 90..... | 38 | 13 | From 80 to 90..... | 16 | From 80 to 90..... | 16 | From 80 to 90..... | 11 | 2 | From 80 to 90..... | 33 | 1 | From 80 to 90..... | 33 |
| | 2 | Dyspnea..... | 5 | 4 | Dyspnea..... | 4 | Dyspnea..... | 17 | Dyspnea..... | 22 | 1 | Dyspnea..... | 11 | 1 | Dyspnea..... | 25 |
| Accompanying conditions | 2 | Exophthalmic..... | 5 | 2 | Exophthalmic..... | 2 | Exophthalmic..... | 3 | Exophthalmic..... | 0 | 1 | Exophthalmic..... | 11 | 0 | Exophthalmic..... | 0 |
| | 1 | Insomnia..... | 3 | 0 | Insomnia..... | 0 | Insomnia..... | 11 | Headaches..... | 15 | 0 | Headaches..... | 42 | 0 | Headaches..... | 0 |
| | 1 | Diabetes..... | 3 | 0 | Diabetes..... | 0 | Diabetes..... | 8 | Pressure..... | 10 | 3 | Pressure..... | 68 | 2 | Pressure..... | 50 |
| | 6 | Tachycardia..... | 15 | 21 | Tachycardia..... | 20 | Tachycardia..... | 39 | Tachycardia..... | 20 | 4 | Tachycardia..... | 58 | 2 | Tachycardia..... | 50 |
| | 1 | Tremor..... | 3 | 0 | Tremor..... | 0 | Tremor..... | 9 | Tremor..... | 12 | 1 | Tremor..... | 11 | 1 | Tremor..... | 25 |
| | 29 | Nervousness..... | 99 | 85 | Nervousness..... | 79 | Nervousness..... | 53 | Nervousness..... | 87 | 4 | Nervousness..... | 38 | 2 | Nervousness..... | 50 |
| Respiratory rate | 2 | Unknown..... | 6 | 28 | Unknown..... | 29 | Unknown..... | 54 | Unknown..... | 59 | 2 | Unknown..... | 28 | 3 | Unknown..... | 25 |
| | 26 | Known..... | 94 | 80 | Known..... | 80 | Known..... | 46 | Known..... | 59 | 5 | Known..... | 76 | 1 | Known..... | 25 |
| | 2 | From 10 to 20..... | 5 | 7 | From 10 to 20..... | 9 | From 10 to 20..... | 11 | From 10 to 20..... | 5 | 1 | From 10 to 20..... | 20 | 0 | From 10 to 20..... | 0 |
| | 2 | From 20 to 30..... | 5 | 27 | From 20 to 30..... | 27 | From 20 to 30..... | 39 | From 20 to 30..... | 38 | 8 | From 20 to 30..... | 20 | 1 | From 20 to 30..... | 100 |
| | 1 | From 30 to 40..... | 3 | 17 | From 30 to 40..... | 21 | From 30 to 40..... | 20 | From 30 to 40..... | 21 | 1 | From 30 to 40..... | 20 | 0 | From 30 to 40..... | 0 |
| | 1 | From 40 to 50..... | 5 | 17 | From 40 to 50..... | 15 | From 40 to 50..... | 20 | From 40 to 50..... | 15 | 0 | From 40 to 50..... | 0 | 0 | From 40 to 50..... | 0 |
| | 29 | From 50 to 100.... | 82 | 22 | From 50 to 100.... | 27 | From 50 to 100.... | 11 | From 50 to 100.... | 19 | 4 | From 50 to 100.... | 10 | 0 | From 50 to 100.... | 0 |
| | 20 | Hyperplastic toxæmia..... | 96 | 29 | Hyperplastic toxæmia..... | 26 | Hyperplastic toxæmia..... | 5 | Hyperplastic toxæmia..... | 1 | 2 | Hyperplastic toxæmia..... | 28 | 1 | Hyperplastic toxæmia..... | 25 |
| Average weight | 1 | Exophthalmic..... | 2 | 5 | Exophthalmic..... | 2 | Exophthalmic..... | 1 | Exophthalmic..... | 0 | 0 | Exophthalmic..... | 10 | 0 | Exophthalmic..... | 0 |
| | 1 | Adenoma..... | 2 | 5 | Adenoma..... | 2 | Adenoma..... | 81 | Adenoma..... | 86 | 35 | Adenoma..... | 58 | 2 | Adenoma..... | 60 |
| | 0 | Toxic adenoma..... | 0 | 28 | Toxic adenoma..... | 26 | Toxic adenoma..... | 13 | Toxic adenoma..... | 10 | 1 | Toxic adenoma..... | 11 | 1 | Toxic adenoma..... | 25 |
| | 11 | Undetermined..... | 29 | 25 | Undetermined..... | 25 | Undetermined..... | 37 | Undetermined..... | 21 | 9 | Undetermined..... | 0 | 0 | Undetermined..... | 0 |
| Average weight, 50 gm. | 27 | Determined..... | 24 | 81 | Determined..... | 26 | Determined..... | 63 | Determined..... | 76 | 31 | Determined..... | 100 | 1 | Determined..... | 100 |
| | 26 | Under 100 gm..... | 60 | 26 | Under 100 gm..... | 76 | Under 100 gm..... | 53 | Under 100 gm..... | 61 | 6 | Under 100 gm..... | 86 | 4 | Under 100 gm..... | 100 |
| | 1 | Over 100 gm..... | 4 | 15 | Over 100 gm..... | 24 | Over 100 gm..... | 47 | Over 100 gm..... | 37 | 12 | Over 100 gm..... | 11 | 0 | Over 100 gm..... | 0 |
| | | Average weight, 50 gm. | | | Average weight, 50 gm. | | Average weight, 50 gm. | | Average weight, 50 gm. | | | Average weight, 50 gm. | | | Average weight, 50 gm. | |

adenomatous hyperplasia), 41 in Group 4 (solitary adenoma with hyperplasia), seven in Group 5 (neoplasm) and four in Group 6 (inflammatory processes). It may be noted that 216, or 70 per cent., fall in the second and third groups.

Age.—Seventy-six per cent. of all the thyroid disturbances came to clinical attention before the fifth decade of life.

The data at hand point to an earlier manifestation of irregularities in Group 1, and in all other groups in proportion to the amount of histologic changes of a similar parenchymatous nature. The age at which

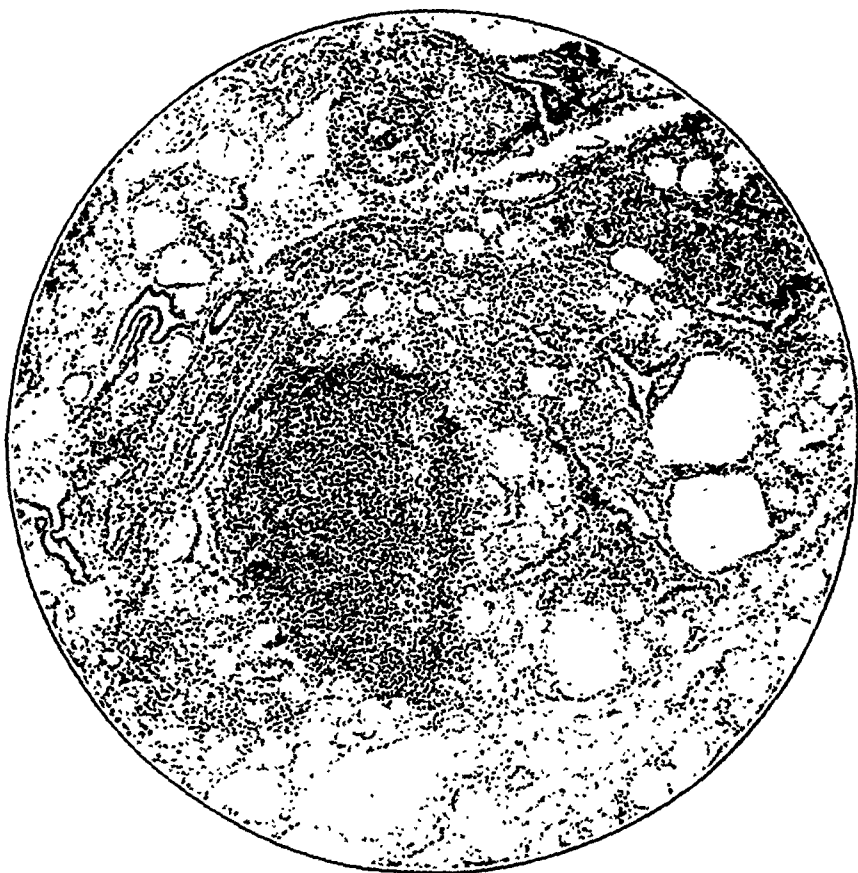


Fig. 2.—Formation of lymph cell collections or pseudolymph nodes in the presence of continued or receding activity.

a patient comes to be treated is of course no criterion as to the time or rate of development. Nodularity in thyroid enlargement evidently requires time, probably being the resultant of many unbalances between storage and the circulatory dispersion of the thyroid hormone.

Sex.—In the first two groups there were four times as many females as males. In two of the groups (Groups 3 and 4), the ratio of males to females is approximately 1:10. The proportion here established shows the relationship in the decades of life in which reproduction is most common, the frequency of thyroid enlargement being greatest in

women. The evidence as to sex ratios, in this study, is at variance with other reports from this district concerning men and women of an earlier age. Hall,¹⁶ examining 3,339 students at the University of Washington, found "perceptible, medium and large" thyroids in 374 men out of 2,086 examined (17.94 per cent.) and in 388 women out of 1,253 examined (30.94 per cent.), respectively, a ratio of one man to two women. The average age was about 20 years.

Location.—Most of the patients studied came from regions in Oregon and Washington. It is generally agreed that thyroid disturbance is

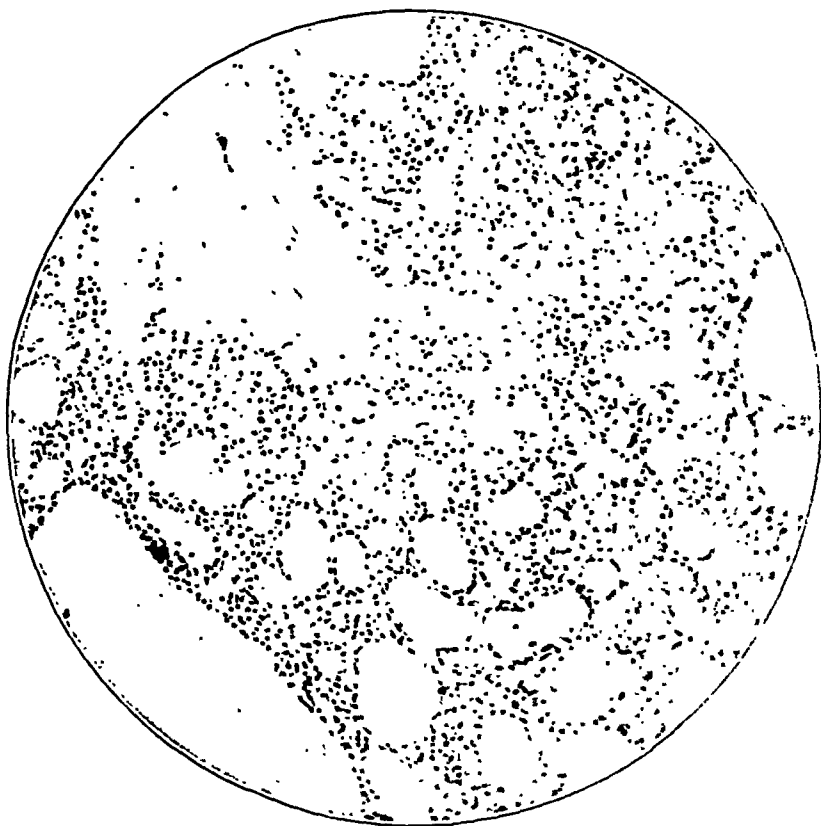


Fig. 3.—Area of adenomatosis near an old scar; such histologic changes are common in regions of the pseudocapsule of nodules or foci of degeneration.

endemic in these two states. It is therefore of interest to note that 12.6 per cent. of all those studied fall definitely in Group 1 (so-called exophthalmic goiter). All gradations between the diffuse parenchymatous hyperplasia group and that of the diffuse adenomatous hyperplasia have been observed. But the incidence of typical so-called exophthalmic goiter given here is of import. There is a scarcity of figures in the literature as to the frequency in nongoitrous districts, so that comparison is not

16. Hall: Northwest Med. 6:189-193

possible. Mortality statistics are unreliable for purposes of conclusions as to the prevalence of a given type in a particular community since the death rate was much higher at that time in the so-called exophthalmic variety than in others.

Rate and Time of Development.—Our clinical histories are incomplete concerning this data. In the first two groups a large percentage developed more rapidly than in those of the other groups. It would be of general interest to know the exact details of the manifestations of

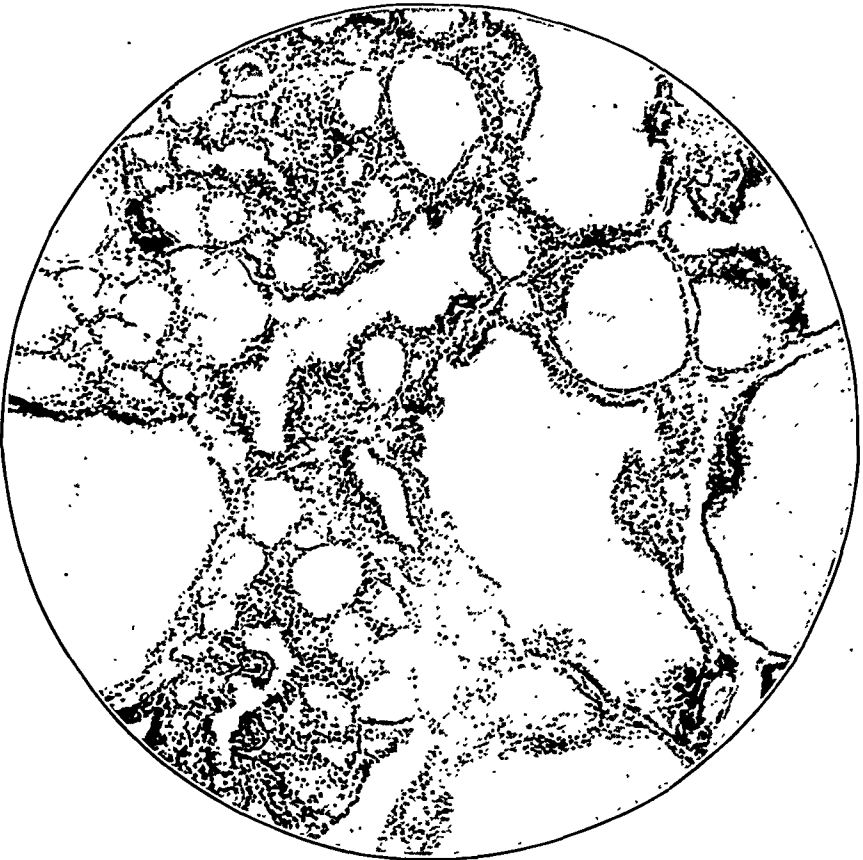


Fig. 4.—Multiple cells lining alveoli and papillary projections.

enlargement that have occurred in each subject presenting himself for treatment.

Marital State.—Approximately 80 per cent. of all the thyroid diseases studied occurred in persons who were married. This high incidence is due to the greater frequency of such disturbances in women who have undergone pregnancies. About half the married women in this series had from one to four pregnancies, in addition to a considerable number of miscarriages. The latter were more frequent in the first two groups. It is probably the result of a combined excessive or modified metabolism and other internal secretion derangements that excite the thyroid in maternity.

Previous Conditions.—Here we have grouped various childhood diseases and incidental infections. All these have induced periodic demands for excess metabolism. It is not possible to pick any one or any group of conditions which may be specifically related to thyroid disturbances. The literature is silent on their rôle. It seems to us that there is to be found here a fertile field for experimentation. There is some suggestion of slow incipient infections, such as tonsillitis, having a more profound and subtle effect on thyroid unbalance than the more acute ones. And

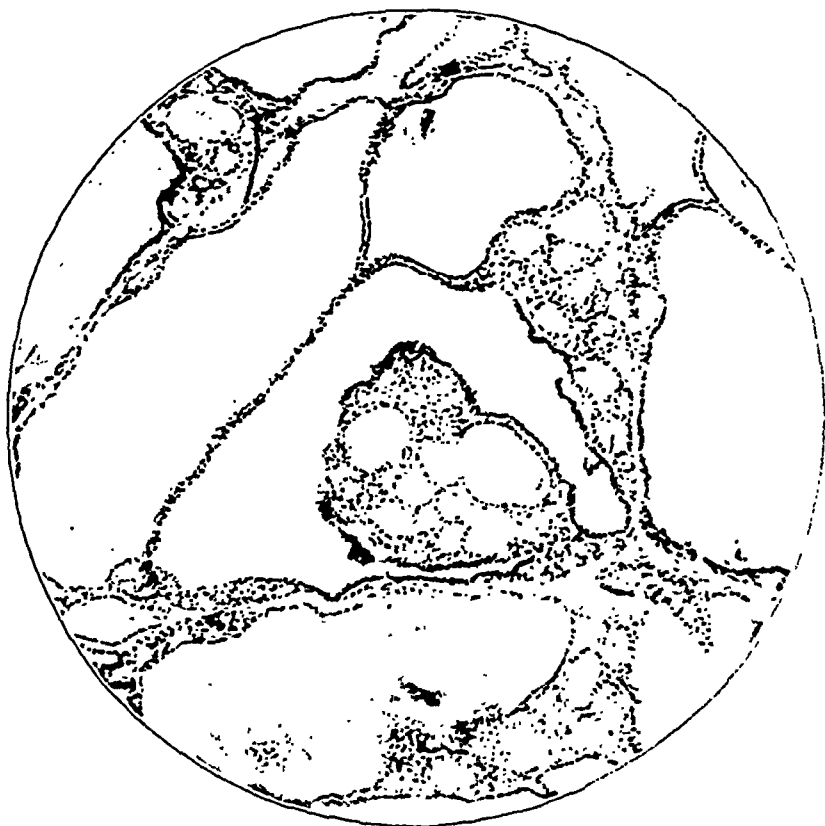


Fig. 5.—Interalveolar hillocks in receding activity.

yet one hesitates to speculate on the appearance of the disturbance in relationship to the time of insults, physiologic or pathologic.

Circulatory Disturbances.—Blood pressure was in general increased. The systolic pressure appeared to have no definite relationship to the type. In respect to the age it was generally higher in the first two groups. In Groups 3 and 4, made up largely of older individuals, such changes as arteriosclerosis and arteriocapillary fibrosis were undoubtedly factors in the average high systolic pressure. In general the pulse pressure is high. In Group 1, 75 per cent. were more than 60; this high average decreased in the other groups. Pulse pressure is apparently much more pronounced in the thyroids exhibiting parenchymatous hyperplasia.

Associated Conditions.—The symptomatology is essentially the same in all types of the disturbances studied, varying only in degree. Dyspnea, tachycardia, nervousness and pressure are the most constant. Diabetes occurred in one instance in the first group. Exophthalmia was seen in the first three groups. It may manifest itself in any thyroid disturbance and is usually associated with emaciation, pointing to excessive metabolism and perhaps other internal secretion disturbances.

Basal Metabolism Rate.—In Group 1 twenty-nine, or 82 per cent., were above plus 50, from three to eight times as high as in any other group. In practically all the instances studied it was above normal (i. e., plus or minus 0 to 15).

Clinical Diagnosis.—Ninety-six per cent. of Group 1 (diffuse parenchymatous hyperplasia) were classified clinically as hyperplastic toxic goiters. This term was applied in 36 per cent. and 5 per cent. of the thyroids in Groups 2 and 3, respectively. Exophthalmic goiter was the diagnosis in a small percentage in the first three groups. Eighty-one per cent. of Group 3 (nodular adenomatous hyperplasia) were classified clinically as toxic adenomas. The clinical classification made independently, at the time of operation, corresponds reasonably well with the natural but somewhat arbitrary pathologic classification adopted here.

Amount Removed.—There has always been more or less speculation as to the effect of the surgical removal of a part of the gland in a given condition. This procedure allows the surgeon to estimate the amount to be removed leaving as far as possible a symmetrical neck. The amount removed is based on the irregularity in size, the evident pathologic condition, and the severity of the symptoms. No two surgeons follow the same technic. In 1898 and later in 1914 Halstead¹⁷ studied the effect of transplantation, removal and amputation of the thyroid gland. He found that the remaining portion of the gland was almost invariably followed by enlargement. The histologic changes were similar to those found in so-called exophthalmic goiter. No such opportunity is afforded clinically. However, the thyroid tissue was weighed immediately after removal and before preservation.

This was done with the idea of checking the end-results in the light of the amount removed and the evidence of disease in the gland. In general, the amounts excised at the present time are smaller than they were several years back, but larger in proportion to the total size of the gland. This is probably because of the education of the public to the dangers of prolonged intoxication from thyroid disturbances and to the need of early consultation of a physician. The amounts removed were smaller in Group 1 and greatest in Group 4.

17. Halstead: Am. J. M. Sc. 147:56, 1914.

In the foregoing discussion, Groups 5 and 6 were not considered because the number of cases are insufficient to warrant the drawing of conclusions. Six of the neoplasms were carcinomas. One was a solitary papilloma. Of the four inflammatory processes two were tuberculous and two were undetermined, but were associated with chronic pharyngeal and peritonsillar disturbances.

The value of any pathologic classification, from a practical point of view, is valuable only as it may be readily fitted into a clinical concept. It has been of interest to us to note that there are many difficulties in such assorting of thyroid diseases, but that the situation approaches futility when there is an attempt made to give each detail in the morbid anatomy a distinctive entity. Until more exact physiologic knowledge is at hand the clinician and pathologist must content themselves with a comparison of the evidences of disease in the patient and the anomalies of thyroid design as seen in the laboratory. Accurate histories as to the time and rate of development as well as careful postoperative observations would add valuable information not found in the literature. We deprecate the use of a simple clinical sign or symptom in naming a certain thyroid disease or type. For example, it is evident in the literature as well as in our study that exophthalmia may be accidental in any hyperthyroidism and yet many clinicians still use it in a specific way. We are in sympathy with the appellations of toxic and nontoxic as introduced by Plummer and Wilson. These terms should, however, be borne out by an accurate clinical record before being applied. More careful accounting of the preoperative facts will undoubtedly lead to a closer agreement between clinical symptomatology and the subsequent studies of the morbid anatomy of the thyroid.

CONCLUSIONS

1. A simple clinicopathologic study is desirable in all thyroid diseases.
2. The incidence of so-called exophthalmic goiter (diffuse parenchymatous hyperplasia) in proportion to other types in endemic and non-endemic areas is of importance.
3. Pregnancy is a factor in precipitating thyroid unbalance. Miscarriages are frequent in proportion to the toxicity.
4. The pulse pressure in thyroid disturbances is usually high, being highest in the parenchymatous hyperplasia group. It is out of proportion to the ordinary changes in blood vessels occurring in early and middle life.
5. The basal metabolic rate is a valuable indicator of thyroid unbalance and should be employed after operative procedures as well as before.

6. More experimentation is desirable in determining the significance of adenomatosis, solitary adenoma and other pathologic changes, as well as the clinical effect of the amount removed.

7. A simple classification of the pathology of thyroids is given because a complicated classification of thyroid disease is futile and cannot lead to knowledge that lies in the field of proper experimentation.

SITUS INVERSUS VISCERUM

AN ANATOMIC STUDY *

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Situs inversus viscerum is that condition in which the normal arrangement of the viscera is reversed to form a mirror picture of the usual position. Such transposition is usually total but may in rare instances involve either the thoracic viscera or the abdominal viscera alone.

The subject has fascinated the medical profession for more than three centuries. There is a certain romantic distinction conferred on a person who differs so fundamentally in the arrangement of his anatomy from his fellow men.

HISTORY

A brief historical survey shows a case of reversed liver and spleen reported by Fabricius in 1600. Petrius Servius, in Rome, in 1643 recorded a case of transposed viscera. In 1824 the condition was recognized for the first time by a clinician. It was discovered by auscultation and percussion, recently acquired aids to clinical examination.

From this time forward the condition has been reported with increasing frequency. In 1865, Grüber reported seventy cases which he had been able to compile up to that date. Küchenmeister¹ in 1884 compiled 149 cases, only forty of which appeared before 1819. Various other writers have added to this series, notably Pic, in 1895, who brought the number up to 190. In 1906 Sorge² was able to compile only 194 cases. In 1912 the literature was reviewed by Karashima.³ He stated that more than 200 cases were probably on record and many others had doubtless been recognized but not reported.

From 1912 forward I have reviewed the literature and present what I believe to be a complete bibliography of the subject from that year up to the end of 1924, thereby bringing the history of the subject to date.

* From the department of anatomy, Columbia University College of Physicians and Surgeons.

1. Küchenmeister, G. F. H.: Die angeborene vollständige seitliche ver-
langung der eingelege des Menschen, Leipzig, 1883.

2. Sorge, F. G.: Kasuistischer Beitrag zur Kenntnis des Situs viscerum
inversus, Thesis, Berlin, 1906.

3. Karashima, I.: Ein Fall von Situs inversus viscerum totalis, Thesis,
Munich, 1912.

The important milestones passed in the history of situs inversus are:

1. The report of the first human cases by Fabricius and Servius, 1606 and 1643.
2. The first clinical observation of the condition in 1824, using auscultation and percussion.
3. The first diagnosis of the condition by roentgenograph in 1897.

It is interesting to note the change in case reports over this long period of years. Of the seventy odd cases reported by Grüber up to 1865, only five or six had been reported in living subjects. Until 1900



Fig. 1.—Thoracic and abdominal cavities reveal transposition of viscera: the heart lies to right in its intact pericardial sac; the liver occupies the left hypochondrium, while the greater part of the stomach lies to right of midline in right hypochondrium; the omentum overlies remaining gastro-intestinal tract, concealing its position.

the vast majority of cases were discovered post mortem or were revealed in the course of surgical exploration of the abdomen. Since that date the number of cases discovered by clinical observation has rapidly risen to a point where they form the great bulk of the case records. This is probably because of the greater frequency of routine physical examination and the wider application of roentgenology as a diagnostic procedure. More than 90 per cent of the case reports at the present time deal with the living subject.

It is not possible to determine with absolute accuracy the number of cases of situs inversus that have been reported. Many authors report



Fig. 2.—Thorax showing relation of structures in superior part of interpleural space: the retraction of the mediastinal parietal pleura on either side reveals the phrenic nerves lying between the pleura and the intact pericardium; the right innominate vein runs obliquely and to the left, in front of the three main branches of the aorta; this vein formed by the junction of the right subclavian and the right internal jugular veins joins the short left innominate trunk, 2 cm. in length, to form the left superior vena cava. The left superior cava extends downward, receiving a pericardial investment to enter the left atrium. Its extrapericardial course is 5 cm. in length and its intrapericardial course about 2.5 cm. The aortic arch covered by the fibrous pericardium is seen extending upward, backward and to the right, giving off the following branches in order from left to right: (1) the innominate, which subsequently divides into left common carotid and left subclavian arteries; (2) the right common carotid artery, and (3) the right subclavian artery. These vary in no way from the usual arrangement except for the transposition.



Fig. 3.—Open pericardial sac showing right ventricle forming apex of heart, situated about 6.25 cm. to right of midline; the left ventricle lies to front and forms greater part of left and inferior borders of heart; the left atrium has opening into it the superior vena cava and the inferior vena cava, which passes through diaphragm to left of midline. The right atrium posteriorly has the openings of the four pulmonary veins. The transverse sinus, indicated by probe, behind the arterial mesocardium is present without variation aside from the fact that its anterior boundary is the pulmonary artery on the right and the aorta on the left, owing to the transposition. The ascending aorta extends upward from the right ventricle between the superior cava on the left and the pulmonary artery on the right. The first 4 cm. of this vessel lies within the serous pericardium while the entire vessel to the arch is covered by the fibrous pericardium. The ascending aorta turns backward and to the right to form the aortic arch described above.

one or more cases and add additional cases from other clinics or from their colleagues. This leads to considerable reduplication, which must be guarded against. As far as can be determined with reasonable accuracy, since 1912 there have been recorded some 160 cases of situs inversus, which brings the number reported by Karashima at that date up to an approximate total of a little less than 400.

FREQUENCY

The condition is now generally regarded as less rare than it was formerly believed to be, but we are not convinced that it is as frequent as some writers imply.

In 1902 when Arneil⁴ wrote on the subject, he communicated with nineteen prominent internists and five anatomists in an effort to compile the number of cases each had seen. Five internists and four professors of anatomy had never seen a case.

Roentgenologists are rather apt to see a larger proportion of the total number of cases than clinicians or anatomists. In response to a letter written by Upson⁵ of Battle Creek to thirteen roentgenologists in 1921, the number which each stated that he had seen was rather vague. Some of them had never seen any. LeWald⁶ at that time stated that he had seen twenty-two cases and in a recent report presented twenty-nine cases that he himself had observed. He admits that the frequency of twenty-nine cases in 40,000 examinations, or 1 in 1,400, is high and we are inclined to agree that his experience has been unusual.

In the anatomic laboratory of the Columbia University College of Physicians and Surgeons during a period of forty years about 10,000 subjects have been examined in routine dissection and the case presented here is definitely the first instance of complete or partial transposition of the viscera; in the years preceding 1885 we have no record of any similar case.

Sherk⁷ stated in 1922 that the Mayo Clinic could find only ten cases out of 347,000 registered in the twelve year period preceding. A report of the frequency of this condition among the recruits of the various armies recently mobilized would have been extremely interesting, but in reply to a recent inquiry the Surgeon General's Office stated that there were no data available on this subject.

4. Arneil, J. R.: Clinical Observations on Congenital and Acquired Transposition of Viscera, *Am. J. M. Sc.* **124**:885, 1902.

5. Upson, W. O.: A Case of Situs Inversus, *J. Mich. M. Soc.* **17**:362 (Sept.) 1918; Transposed Viscera, *Am. J. Roentgenol.* **8**:385 (July) 1921.

6. LeWald, L. T.: Complete Transposition of the Viscera, *J. A. M. A.* **84**:261 (Jan. 24) 1925.

7. Sherk, H. H.: Total Transposition of Viscera, *Surg., Gynec. & Obst.* **35**:53 (July) 1922.

While the condition is doubtless recognized more often at the present time than formerly, we are in no position to discuss its frequency with certainty.

THE INDIVIDUAL

A great deal has been written concerning the individual possessing this unusual arrangement of the viscera. One writer stated that he has seen seven patients, all of whom were in poor health. It is at times reported that the individual with the inverted situs is left handed. Two reports were noted in which the condition existed in two brothers and



Fig. 4.—The heart lifted out of its pericardial sac with the oblique sinus of the serous pericardium exposed, extending upward to the left; the orifice is bounded below and to the left side by the inferior vena cava and above to the right by the right pulmonary veins.

one in a brother and a sister. One roentgenologist reported four cases in the same family.

The majority of case reports, however, show that the individual differs not at all from the ordinary human being. He does not seem to be left handed more frequently than his fellows. He is apt to live his life unmarked by any peculiarity and die of the same diseases that carry off the rest of mankind. There is no proof that heredity plays a part in



Fig. 5.—Termination of thoracic duct: the duct passes upward in the superior mediastinum from behind the aortic arch, behind the right subclavian artery; passing into the neck it curves outward, upward and to the right, behind the right vagus nerve, the right common carotid artery and the right internal jugular vein; it passes in front of the right subclavian artery and the vertebral artery and vein; it terminates in a bulbus enlargement that empties into the junction of the right subclavian and the right internal jugular veins, lying directly in front of the medial margin of the scalenus anterior and the phrenic nerve. The right vagus nerve is shown retracted with the thoracic duct passing upward and outward between the retractors to disappear behind the right internal jugular vein; its terminal enlargement and cardiac branches of the cervical sympathetic trunk crossing in front of the duct can readily be seen.

this condition. The European case reports usually end with the observation that the individual was quite fit for military duty.

ETIOLOGY

The theories as to etiologic factors in this condition are numerous. The following are some of the views that have been held:

1. The persistence of a right omphalomesenteric vein influencing the shifting of the stomach to the right instead of to the left.



Fig. 6.—Left vagus nerve and its recurrent branch; this branch arises in front of the left subclavian artery and winds from before backward around that vessel, ascending obliquely behind the left common carotid artery and behind the inferior thyroid artery to the groove between the trachea and the esophagus.

2. The influence of the umbilical cord. In situs inversus it is wound spirally to the right instead of to the left. The blood column flowing in the reverse direction is responsible for the turning of the heart to the

opposite side. It is difficult to understand how the blood column in the umbilical vein, after passing through the liver, could exert much force. This theory seems utterly untenable.

3. The turning of the embryo to the right side of the umbilical vessels instead of to the left as it normally lies.

The relation of situs inversus to anomalies of the abdominal veins, from the etiologic standpoint, has been studied extensively by von



Fig. 7.—Right vagus nerve and its recurrent branch; the latter nerve arises from the vagus to the right of the aortic arch and passes backward, then upward behind the arch to ascend along the side of the trachea, between it and the esophagus.

Werdt.⁸ In a careful survey of a large number of case reports of situs inversus he noted the anomalies of the abdominal veins, and concluded that the embryology of the venous system afforded no constant explana-

8. Von Werdt, Felix: Zur Kenntnis des Situs inversus unter der mit demselben häufig verbundenen Anomalien im Bereiche der grossen Abdominal venen, *Arch. f. mikr. Anat.* 95:37, 1921.

tion of the etiology of situs inversus, because most of these variations developed after the reversed asymmetry of the viscera had been determined.

The existence of situs inversus in certain types of monsters has long been recognized. Morrill's⁹ study of symmetry reversal and mirror imaging in monstrous trout, with a comparison of a human dicephalic monster, is an interesting piece of work. This author has compiled six cases of these dicephalic monsters presenting a reversed visceral asymmetry of one of the components. He states that there is a general agreement that transposition of viscera does not occur in duplicate twins. The question is raised by Morrill why mirror imaging occurs occasionally, but not always, in certain types of monsters.

Wilder's¹⁰ investigation of duplicate twins and double monsters is interesting but not entirely satisfactory in an attempt to interpret the results in terms of etiology of transposition of viscera. This author found that double monsters show all degrees of mirror imaging but that duplicate twins presented only vestiges of such. In a small number of cases investigated he found in a majority a reversal of the index finger pattern. The pattern of the right index finger of twin A was the mirror image of the left index finger pattern of twin B. This symmetry reversal is emphasized as evidence of the single ovum origin of these individuals and interpreted as the lost trace of an earlier more general mirror imaging which has been subsequently outgrown.

Newman,¹¹ in his study of armadillo quadruplets, found that there was no reversal of asymmetry of the viscera but that there is a reversal of the pattern in the tegumentary system. He concludes that there is so little tendency to mirror imaging in duplicate human twins and so much in the armadillo because the human twins become isolated at a considerably earlier period than the armadillo quadruplets. He states that the earlier the separation takes place the more complete is the reorganization of symmetry relations in the separated individuals and the less is the residuum of the common mirror symmetry. Double monsters begin to separate comparatively late in ontogeny and therefore show pronounced mirror imaging.

These observations are of great interest but they fail to explain the basic cause of the situs inversus viscerum. We must pursue a more

9. Morrill, C. U.: Symmetry Reversal and Mirror Imaging in Monstrous Trout and Comparison with Similar Conditions in Human Double Monsters, *Anat. Record* 16:265, 1919.

10. Wilder, H. H.: Duplicate Twins and Double Monsters, *Am. J. Anat.* 3, 1904; Morphology of Cosmobia, *ibid.* 8, 1908; Palm and Sole Studies, II, *Biol. Bull.* 30:135, 211, 1916.

11. Newman, H. H.: Heredity and Organic Symmetry in Armadillo Quadruplets, *Biol. Bull.* 30:173, 1916.



Fig. 8.—Right pleural cavity and lung: the single primary oblique fissure is seen dividing the lung into two lobes, an upper and a lower lobe; the fissure extends from the upper and posterior part of the hilum to the costal surface, from about 5 to 6 cm. below the apex, and then continues downward and forward to the inferior border where it is situated about 4 cm. behind the anterior extremity of that border. It then extends upward to the inferior margin of the hilum. The right pleural cavity contained several hundred cubic centimeters of thick turbid pus and the diaphragmatic and costal pleurae are much thickened and covered with fibrinous plaques as is the interlobar visceral pleura, showing the suppurative pleurisy suggested in the clinical note of Dec. 13, 1921.



Fig. 9.—Left pleural cavity and lung; the pleura was shiny and glistening throughout. The arrangement of lobes and fissures is interesting: the primary oblique fissure extends from the upper part of the hilum to the costal surface at a point about 6 cm. below the apex; it extends obliquely downward and forward 7.5 cm. to a point on the lateral costal surface where it is joined by the transverse fissure; it continues its course to the inferior margin where it terminates 7 cm. below and behind the anterior extremity of that border. The transverse fissure commences on the anterior margin 6.5 cm. above its lower extremity and runs upward and outward to intersect the oblique fissure and is then carried laterally, incompletely subdividing the inferior lobe into a superior and inferior portion. This approaches the frequently recorded variation of four lobes in the right lung. In this case the left lung shows three complete lobes and a fourth incomplete at the expense of the inferior lobe. The two additional grooves shown at the lower part of the inferior lobe are merely impressions that do not in any sense approach the semblance of fissure. The vena azygos, receiving the left superior intercostal vein, arches over the root of this lung.

fundamental search in any effort to determine the causes of this condition.

Zurstrassen¹² observed, in his studies of *Ascaris megalocephalus*, that in the eight cell stage one egg out of every thirty or forty showed the inverted situs and that four of 125 adults similarly presented reversed asymmetry of the viscera. He decided that the asymmetry of the embryo present in the eight cell stage was probably responsible for the adult situs inversus.



Fig. 10.—Detailed view of left upper quadrant of abdomen or left hypochondrium: the liver, of normal size, is divided into a large left and a smaller right lobe by the sulcus into which passes the falciform ligament with the obliterated umbilical vein in its free margin. Beneath the left lobe of the liver lies the gallbladder and from the porta hepatis passes the lesser or gastro-hepatic omentum, downward and to the right to the lesser curvature, or left border, of the stomach, the epiploic foramen of Winslow is seen behind the left extremity of the lesser omentum.

Crampton¹³ showed among certain gasteropods a correlation between the position of the organs and the segmentation pattern. The usual type of asymmetry with a dextral shell is associated with a spiral cleavage

12. Zurstrassen, O. L.: Embryonal Entwicklung der *Ascaris Megalocephalus*, Arch. f. Entwicklungsmechn. d. Organ 3:27, 1896.

13. Crampton, H. E.: Reversal of Cleavage in a Sinistral Gasteropod, Ann. New York Acad. Sc. 8:167, 1894.

to the right. Other forms such as *Physa*, however, have a sinistral shell with reversed asymmetry of the viscera and a reversal of cleavage. The first evidence of variation appeared at a late two cell stage.

There are some observations that suggest that in the vertebrates also the factors for reversed asymmetry may be present in early developmental stages.

Perhaps the most interesting investigations on the subject dealing with vertebrate material are those of Spemann¹⁴ and later of Pressler,¹⁵ working with *Bombinator igneus* and *Rana esculenta* during the neurula stage, they excised a square of the medullary plate with a portion of the primitive foregut and rotated it 180 degrees so that the original cephalic end was placed caudad. A number of these embryos developed with a complete situs inversus.

Levy,¹⁶ working with *Triton taeniatus*, tried to rotate the heart anlage in a like manner to produce situs inversus but failed because he was unable to isolate it.

The question of what determines the normal asymmetry must be solved before we are in a position to attack the problem of etiology of *reversed* asymmetry of the viscera. From the investigations quoted it seems probable that such asymmetry is not primarily the result of local variation but is due to factors operating at an early ontogenetic period.

We are still in doubt regarding the etiology of this condition, with a number of interesting lines of investigation suggested.

The case presented here was discovered in the dissecting room. In subsequently tracing the body it was found that the condition had been recognized and studied by the clinicians in a hospital of this city, so we are fortunately able to present a rather complete history. The condition is a complete transposition with a variation in the genito-urinary tract, a fused kidney situated entirely in the left umbilical and lumbar regions. The two components of this double organ are easily recognized and the ureters pursue a relatively normal course after passing over the pelvic brim.

REPORT OF CASE

C. T., a man, aged 24, born in Italy, was admitted Nov. 25, 1921, and died Jan. 3, 1922. The final diagnosis was bronchopneumonia, nephroptosis and transposition of the viscera. The chief complaint was that he had had indigestion for eight months.

14. Spemann, H.: Ueber eine neue methode der Embryonal's Transplantation, Verhandl. d. deutsch. Zool. Gesellsch, 1906; Ueber Embryonale Transplantation, Verhandl. d. Gesellsch. deutsch. Naturf. u. Aerzte, 1906.

15. Pressler, K.: Beobachtungen und Versuche über den Normalen und inversen situs viscerum et cordis bei Anurenlarven, Arch. f. Entwcklungsmechn. d. Organ. **32**:1, 1911.

16. Levy, Oskar: Entwicklungsmechanische Studien am Embryo von Triton Taeniatus, Arch. f. Entwcklungsmechn. **20**:335, 1906.

The patient had been well until the onset of the present illness. The past history was negative aside from chancre three years before. After each meal he had distress and an uncomfortable feeling in the epigastrium and gaseous eructations. He had no pain and did not vomit. He had lost weight, and came to the hospital because of acute indigestion.

Physical examination showed a poorly nourished adult, not acutely ill. The eyes and ears were normal, and the mouth, aside from bad teeth. There was



Fig. 11.—Mesenteric root with the ascending and transverse colons retracted, extending from duodenojejunal junction at level of second lumbar vertebra to right of midline, downward to left iliac fossa where terminal ileum is seen emptying into cecum from right to left.

asymmetry of the ribs. Chondrosternal junction did not correspond on the two sides. There was retraction of the supraclavicular and the infraclavicular spaces. Expansion was normal, equal and symmetrical. The lungs were resonant throughout. Breath sounds were normal. The voice and tactile fremitus were normal. No râles were heard.



Fig. 12.—Spleen occupying right upper quadrant or right hypochondrium lying below dome of diaphragm on tenth, eleventh and twelfth ribs. The spleen is in all respects normal, presenting a large gastric surface which supports the right extremity of the posterior surface of the stomach. The splenic flexure of the colon is just visible below the spleen; the descending colon is seen extending through the right lumbar region to the iliac fossa where it becomes the iliac colon. The sigmoid colon, shown in part, is not much over 20 cm. in length and has a relatively short mesocolon; it passes into the rectum from right to left. The right lumbar region with the small bowel retracted reveals no evidence of a right kidney.

In the right fifth interspace the apex was felt 7 cm. to the right of the midline. The first sound at the apex was of good quality and regular in force and rhythm. There were no murmurs. The pulmonic second sound was greater than the aortic second. The pulse was regular in force and rhythm. The systolic blood pressure was 112, the diastolic 70. The arterial walls were not palpable.

The liver was on the left side, the upper border at the fifth rib; the lower border was not felt. The stomach percussed in the right side; the spleen and the right kidney were not felt. In the left lower quadrant, in the region of the kidney, there was a mass that resembled kidney in size and position; it was movable like a floating kidney, very tender, irregular in outline, nodular and did not move with respiration. The abdominal walls were lax. The extremities were negative. Reflexes were diminished. The right testis was lower than the left.

The provisional diagnosis was congenital transposition of the viscera; floating kidney; neoplasm of the left kidney, and neoplasm of the gastrointestinal tract.

Heart Measurements in Centimeters

| Intercostal Space | Right Midsternal Line, Cm. | Left Midsternal Line, Cm. |
|-------------------|----------------------------|---------------------------|
| 2 | 4 | 2 |
| 3 | 6.5 | 3 |
| 4 | 6.5 | 4 |
| 5 | 7.5 | |

Roentgenograms could not be obtained, but the reports are submitted as follows:

November 29, there was noted complete transposition of the viscera; examination of the chest showed moderate emphysema. November 30, examination of the genito-urinary tract revealed no calculus in either ureter. There was some enlargement of the right kidney, and it was moderately ptosed.

November 30, fluoroscopic examination showed the position of the heart to be entirely transposed. The cardiac axis had normal curves, the normal left curves on the right and the normal right curves on the left. No examination of the inner cardiac curves was made. The shape was normal, and there was no definite enlargement. The aorta was normal. The measurements were: maximum transverse, 11.5 cm.; total length, 13.5 cm.; angle of inclination, 41 degrees; broad diameter, 8.9 cm.; width of aorta, second rib, 4.1 cm., and width of pulmonic field, 26 cm.

December 2, examination of the gastro-intestinal tract showed complete transposition of the viscera. The stomach was on the right side of the abdomen. There was no defect in the gastric outline. The bulbous duodeni was filled with difficulty but completely. No gastric retention was noted at the end of six hours. The head of the column was in the cecum, the tail in the ileum. A twenty-four hour examination showed the head of the column in the rectum, the tail in the cecum; haustration was deep and regular; the appendix was visualized 1 inch (2.5 cm.) long, extending inward, and was not tender. There was transposition of the gastric and the gastrocolonic mass in the lower quadrant.

December 6, a cystoscope passed without difficulty. The bladder was emptied of 9 cc. of pale amber urine. The ureteral orifices were normal in position and in appearance, the openings being very small. The bladder texture was normal throughout. Both ureters were catheterized, pale, amber urine being obtained on the left side and a smaller quantity, slightly blood tinged, returned from the right. Six milligrams of phenolsulphonphthalein intravenously injected appeared on each side in three minutes. The specimen was colored for ten minutes. A double pyelogram was made.

A mass in the left upper quadrant just lateral to and above the umbilicus was quite freely movable, shaped like a kidney and rather painful on pressure. No kidney pain was felt in the loins. There were no urinary symptoms and no hematuria. The impression was that the left kidney was movable, and that there was transposition of the viscera.

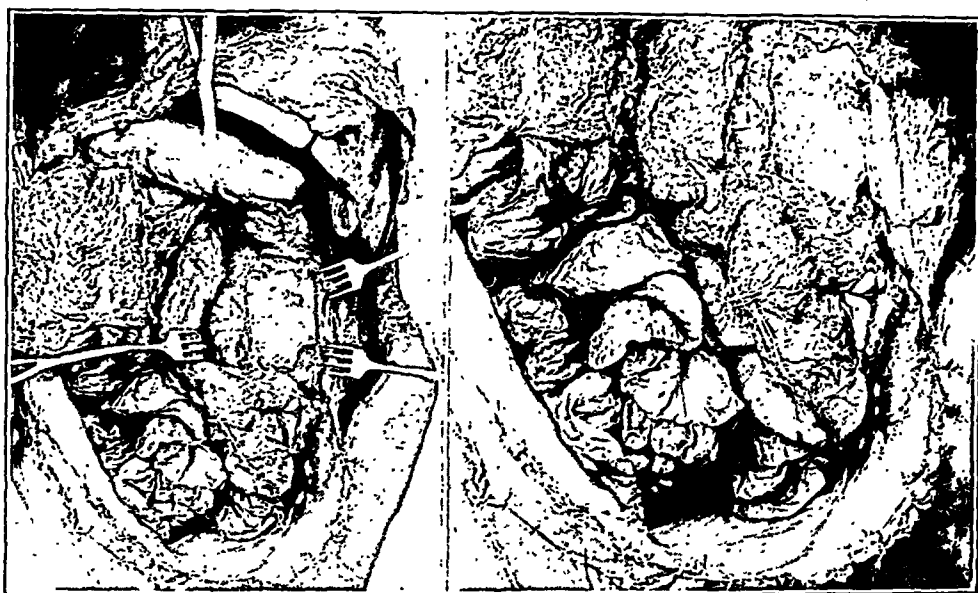


Fig. 13.—The left iliac fossa revealed the cecum with an appendix a little above and behind in the retrocolic position; the appendix grossly was quite normal. Above and behind the appendix and the ascending colon was a large dense mass measuring about 10 cm. in diameter, adherent to the overlying viscera and underlying iliac fossa by dense scar tissue; lying directly beneath the abdominal operative wound, this mass had evidently been the objective of the exploratory operation described in the clinical record of this patient.

The pyelogram showed an opaque catheter present in the left ureter, extending upward and outward from the level of the third sacral segment to a point about 1 cm. above the iliac crest and 7.5 cm. from the midline. The tip of the catheter entered the pelvis from the outer side. There was marked distortion of the pelvis and the calices. The pelvis was divided into upper and lower arms from the extremities of which spring the minor calices.

December 13, at operation a vertical incision 6 cm. long was made through the left rectus abdominis. The ascending colon was found misplaced inward and the omentum was adherent to the large mass under the colon and to its outer side. The posterior peritoneum was opened exposing this mass and revealing a fused kidney with the right kidney calices pointing to the left



Fig. 14.—The dissection exposing the genito-urinary system was difficult because of the dense scar tissue resulting from the operative procedure and the inflammatory process before and after. The dissection was done retro-peritoneally, an attempt being made to preserve carefully the overlying peritoneal structures intact. The renal mass, or fused kidney, consisting of two apposed kidneys each with its own ureter, is shown; the entire lobulated mass measured about 12 cm. in longitudinal and transverse diameter and 4.5 cm. in anteroposterior diameter and was situated in the left iliac fossa, extending from a little to the right of the midline to within 3 cm. of the iliac crest. The right kidney was closely imposed on the left, occupying the right superior aspect of the fused mass with its hilum in front and to the left. The left kidney, somewhat larger, occupied the left and inferior aspect of the mass with its hilum to the left and in front. The right ureter springs from three major calices at the hilum of the right kidney, lying in front of the right renal vein and artery. Commencing at the midline of the body, it passes downward and to the right over the body of the fifth lumbar vertebra, directly in front of the right iliac vein, and over the pelvic brim, down the right lateral pelvic wall to terminate at its usual site. The left ureter springs from four major calices at the hilum of the left kidney, lying to the outer side of the left iliac fossa. The ureter is ventral to the various vascular structures that enter or leave the hilum. It passes over the inferior pole of the left kidney, crosses the external iliac vessels, passing over the pelvic brim down the left lateral wall of the pelvis, is crossed by the ductus deferens, and terminates also at its usual site.



Fig. 15.—Vascular pedicle of fused renal mass showing inferior vena cava, abdominal aorta and various renal vessels; the inferior cava is seen lying to the left of the vertebral column formed by the confluence of the right and the left iliac veins; the abdominal aorta, bifurcating at the level of the body of the third lumbar vertebra and its two terminal iliac branches, is seen to the right of the cava. The following arrangement of the vascular structures of the renal mass is to be noted:

Veins: From the left kidney there emerges (a) a rather large vein from the hilum passing over the lower pole to empty into the left internal iliac or hypogastric vein, shown as the lower vessel in the illustration; (b) a large, short, thick trunk which empties directly into the inferior vena cava; the torn vein and its orifice into the vena cava can be seen; (c) from the lower pole of the right kidney, a vein passes upward and to the right of the fused renal mass to join with a large vein formed by two tributaries from the ventral aspect of the upper poles of both right and left kidneys. This trunk after receiving two or three lumbar veins passes behind the aorta at its bifurcation on the body of the third lumbar vein and empties into the inferior vena cava.

Arteries: (a) the abdominal aorta just before its bifurcation gives off a large renal artery that goes to the upper pole of the renal mass giving branches that end at the hilum of each kidney; (b) the left iliac artery sends a good sized branch to the dorsal aspect of the left kidney; this divides into two large branches which eventually reach the hilum, one, the posterior aspect, and the other, the anterior aspect, passing over the upper pole on the way; (c) the right iliac artery sends a small, short, thick trunk to the lower pole and hilum of the right kidney.

and the kidney body lying over the lumbar vertebrae. To this was attached the left kidney, about twice the size of the right and extending to the left with its calices pointing to the right. The body of the left kidney was readily freed. Three vascular pedicles were found, the first under the hilum, behind the pelvis, the vessels arising at the level of the fourth and the fifth lumbar vertebrae. The third vascular pedicle descended from about the second to the third lumbar vertebra between the fused convex borders of the kidneys. In this pedicle the vein lay in front of the artery.

Focal suppuration was found in the lower pole of the left kidney. The kidney parenchyma and the pelvis were carefully explored for tuberculosis and tumor. A cigaret drain was inserted down to the point of focal suppuration.

December 13, in the right axillary space there was dulness, increased voice and diminished fremitus. Subcrepitant râles were heard in the anterior axillary line. In the posterior axillary line breathing was bronchial though slightly distant. The impression was that the patient had pneumonia with extension to the pleura. Thoracotomy was advised if the temperature continued to fluctuate.

The patient died, Jan. 3, 1922, three weeks after the operation, death being due to sepsis, with localization of suppuration in the fused kidney and a large collection of pus in the right pleura.

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THE MECHANISM OF LOCALIZATION OF GAS IN THE PLEURAL CAVITY AND ITS CLINICAL APPLICATION IN PNEUMOTHORAX THERAPY*

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Thoracoplasty has rightly been considered as a further development of artificial pneumothorax in the surgical treatment of pulmonary tuberculosis, the prime purpose of each being to put the diseased lung at rest. However, in the light of our newer understanding of the localization of gas in the pleural cavity with relation to the diseased and nondiseased portion of the treated lung, thoracoplasty cannot be considered to parallel artificial pneumothorax in its mode of action and ultimate effect. In one class of cases at least the action of artificial pneumothorax, if administered in the proper way, is unparalleled by any other method; it enables the complete compression of the diseased portion without affecting the functioning portion of the treated lung. It is best accomplished in persons with a soft lesion of the exudative type of pulmonary tuberculosis limited to one area of the lungs which is more or less free from pleural adhesions.

This gas distribution in the pleural cavity is based on definite biophysical laws and principles of pneumodynamics and should be made use of in every case treated with artificial pneumothorax. A clearer understanding of these pneumodynamic principles would probably lead to a wider application of artificial pneumothorax in early cases of pulmonary tuberculosis before the lesion becomes far advanced, when this therapy, as well as thoracoplasty, is but an ameliorative measure.

MECHANISM OF GAS LOCALIZATION IN PLEURAL CAVITY

The elastic tissue of the lung, like any other elastic substance, possesses both an expansile and a contractile force. Both these forces come into play in the physiologically functioning lung, which is kept expanded in the air tight pleural cavity by virtue of the difference between its intrapleural and intrapulmonary pressures to which it is subjected. The intrapulmonary surface is exposed directly to the atmospheric pressure through its air passages, whereas the rigid wall of the thorax transmits only very little, if any, of the atmospheric pressure to its pleural surface, and the easily distensible alveoli yield therefore to the atmospheric pressure, putting the entire lung on a stretch. The

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* From the Jewish Consumptives' Relief Society Sanatorium.

intrapleural pressure is therefore equal to the atmospheric pressure minus the tension of the expanded lung.

Any force that increases the intrapleural pressure curtails the expansion of the lung, this curtailment being directly proportional to the difference between the intrapleural and intrapulmonary pressures. Air introduced into the pleural cavity naturally increases the intrapleural pressure, but as long as this pressure is below that of the intrapulmonary, the expansibility of the lung will assert itself with each inspiration. When the intrapleural and the intrapulmonary pressures are equalized, both the contractility and expansibility of the lung tissue are in a state of equilibrium.

In my article on the classification of artificial pneumothorax and the clinical value of the several types¹ I discussed in detail how pathologic processes may diminish either the expansibility alone or the contractility alone, or both of these properties might be lost at the same time. In atelectasis the expansile force of the pulmonary tissue is reduced, and the contractile force is present. In hypertrophic emphysema the expansibility is present but the contractility is diminished. In caseous areas of the lung both the expansile and contractile properties are lost entire; consequently such tissue will yield easily to any external pressure to which it might be subjected. Fibrous tissue possesses intrinsic contractile power to some degree, but it is very resistant to external forces. However, once compressed it will never tend to reexpand. A tuberculous lung almost always exhibits all these pathologic processes in various proportions.

When a small amount of air is introduced into the pleural cavity containing a tuberculous lung free from adhesions it will distribute itself according to the degree of resistance offered to it by the various portions of the involved pulmonary tissue. The caseous soft areas are the first to cave in, the edematous and slightly infiltrated tissues follow, whereas the uninvolved elastic lung tissue expands fully with each inspiration and displaces the introduced gas into the area left by the compressed inexpandible diseased portion. Since the upper lobe is affected in the great majority of cases of pulmonary tuberculosis, an erroneous impression was gained by some that gas introduced into the pleural cavity will always compress the apex first. Such, however, is not the case. Due to these biophysical laws of pneumodynamics just explained, gas injected in small amounts will as a rule localize over the diseased pulmonary area, no matter where it be situated, apex, middle portion or base, provided no pleural synechiae are present. The figures illustrate these views clearly.

1. Bendove, R. A.: The Classification of Artificial Pneumothorax and the Clinical Value of the Several Types, *Am. Rev. Tuberc.* 10:540 (Jan.) 1925.



Fig. 1.—Chest showing infiltration and cavitation of right upper lobes.

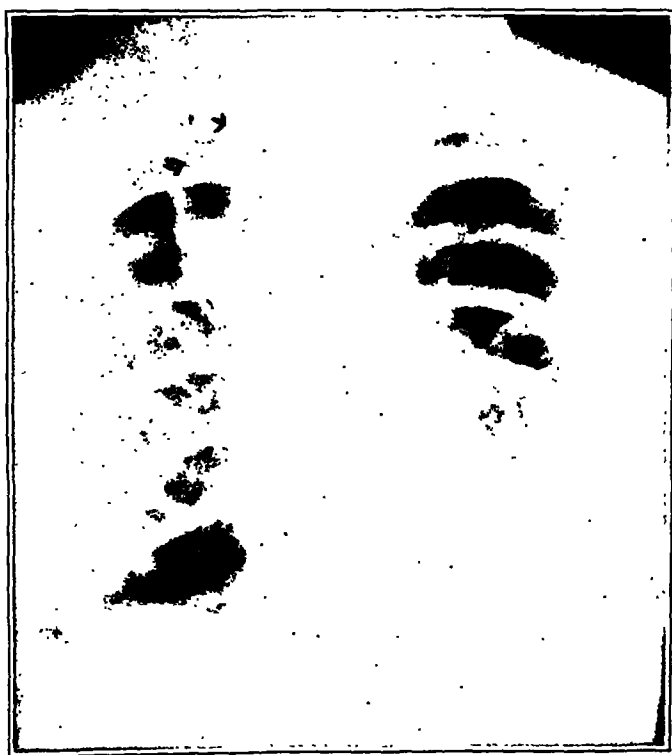


Fig. 2.—Patient shown in figure 1 twenty-four hours after the introduction of 300 cc. of air into the right pleura; the localization of air over the upper diseased area should be noted.

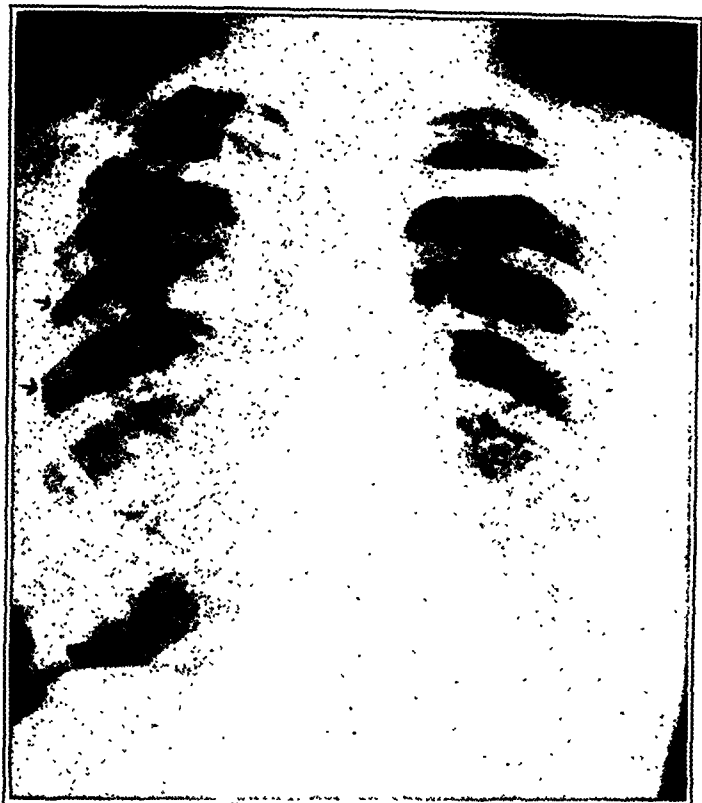


Fig. 3.—Chest of patient shown in figure 1 in inspiration nine days after initiation of pneumothorax; the diseased upper portion is compressed, and the lower functioning portion expands and contracts with the respiratory phases.



Fig. 4.—Chest of patient shown in figure 1 in expiration nine days after initiation of pneumothorax.

Figure 1 is a roentgenogram of pulmonary tuberculosis in which the lesion appears limited to the upper third of the right lung. There is a small cavity in the upper lobe surrounded with soft caseous areas, probably of the exudative type of lesion. Figure 2 is a roentgenogram of the same chest taken a few hours after the introduction of 300 cc. of air into the right hemothorax. The gas has localized itself over the upper diseased area whereas the lower functioning portion of the lung was not affected at all, expanding to its full capacity during inspiration. Figures 3 and 4 are roentgenograms in inspiration and expiration, respectively, taken nine days after the initiation of pneumothorax,

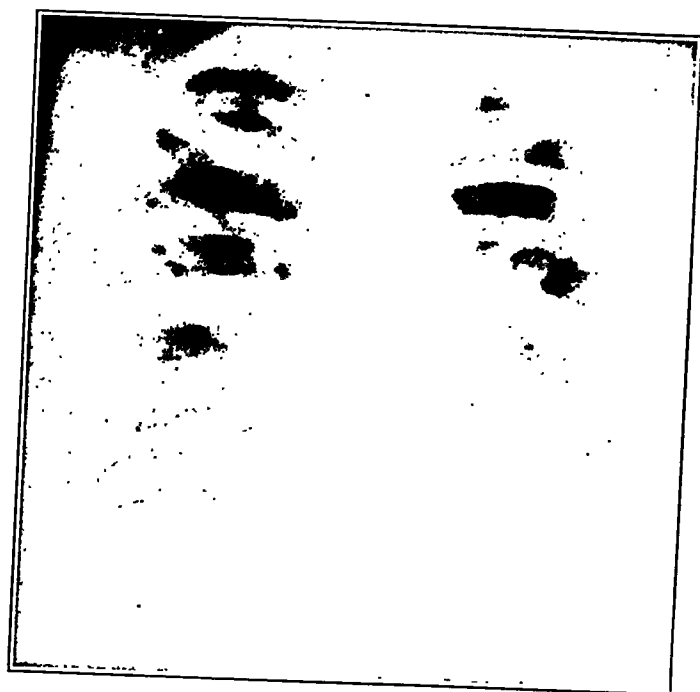


Fig. 5.—Chest showing a confluent caseous area at left base; scattered infiltration in both upper lobes.

during which time two more refills were given, each consisting of 300 cc. Altogether 900 cc. was administered. The intrapleural pressures at this time were —60—20 water manometer. The inspiratory roentgenogram shows that the introduced air has localized itself mostly over the diseased area, reducing it, as well as the cavity, to more than one-half its original size, whereas the unaffected portion of the lung still expands with each inspiration to almost its full capacity, leaving only a narrow slit of pneumothorax at the outer zone. During deep expiration, however, when the volume of the thorax is reduced a great deal in all its diameters, the introduced air could not room itself in the upper part alone, and it naturally distributed itself downward, compressing also the functioning portion of the lung, driving out its residual air,

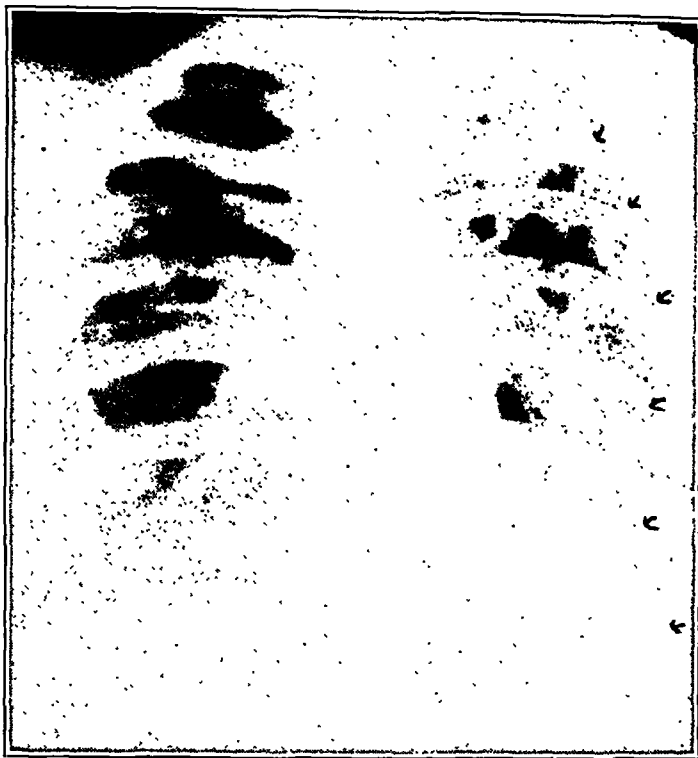


Fig. 6.—Patient shown in figure 5 in inspiration twenty-four hours after introduction of 300 cc. of air; the compressed diseased basal area and functioning upper portion of the left lung should be noted.



Fig. 7.—Patient shown in figure 5 in expiration twenty-four hours after introduction of 300 cc. of air.

which brings about a better ventilation of the lung, as will be discussed later.

Figures 5, 6, 7 and 8 illustrate the same pneumodynamic principles, though here the lesion is at the base. Figure 5, a roentgenogram taken one day before pneumothorax was initiated, shows a dense confluent shadow involving the entire lower third of the left lung. This was interpreted as a soft basal lesion. Three hundred and fifty cubic centimeters of air was introduced and roentgenograms, both inspiratory and

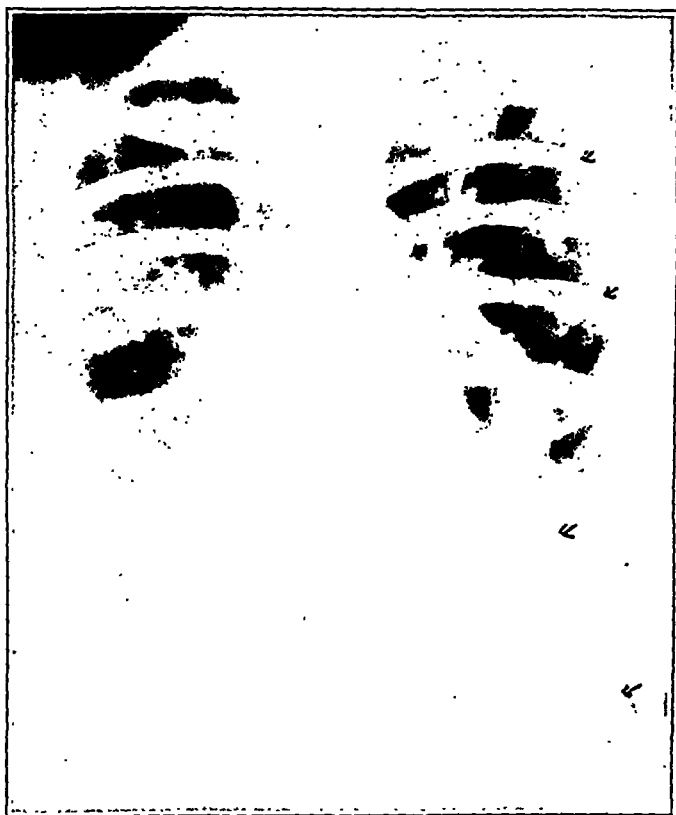


Fig. 8.—Patient shown in figure 5 three months after initiation of pneumothorax; the gas localized mostly over the diseased basal portion, compressing it completely; the upper functioning portion expands with each inspiration.

expiratory, were taken a few hours later. The air is seen to be localized mostly over the diseased basal area, the size of which changes little with the respiratory phases, whereas the upper functioning portion of the lung expands and contracts with each inspiration and expiration. Figure 8 is a roentgenogram taken about three months after the commencement of pneumothorax therapy, and shows the lower diseased portion compressed almost completely, while the upper unaffected portion is expanded almost fully during inspiration.

Figures 9, 10 and 11 bring out the fact clearly that when the lesion is disseminated throughout and affects the entire lung there can be no localization of gas over one area, but the introduced gas distributes itself equally from apex to base, provided there are no adhesions. The prepneumothorax roentgenogram shows a marked infiltration of the entire left lung. The roentgenograms taken a few hours after the introduction of 300 cc. of air show the air to be distributed equally from apex to base, and there is no appreciable change in the extent of



Fig. 9.—Chest showing dense infiltrations of entire left lung.

the collapse in either inspiration or expiration, because in this case the entire lung lost a great deal of its expansile property.

The expansibility of the lung tissue asserts itself only as long as the intrapleural pressure remains lower than the atmospheric pressure, but as soon as the intrathoracic pressure approaches that of the intrapulmonary pressure, the expansile force of the lung is put, as it were, in a state of equilibrium. Consequently, when the intrapleural pressure becomes higher than the intrapulmonary pressure it will not only inhibit the expansibility of the lung, but it also actively compresses it, the degree of compression bearing a direct relation to the increase in positive intrapleural pressures. The localization of the gas in such cases is governed by different dynamic laws, as will be indicated subsequently.

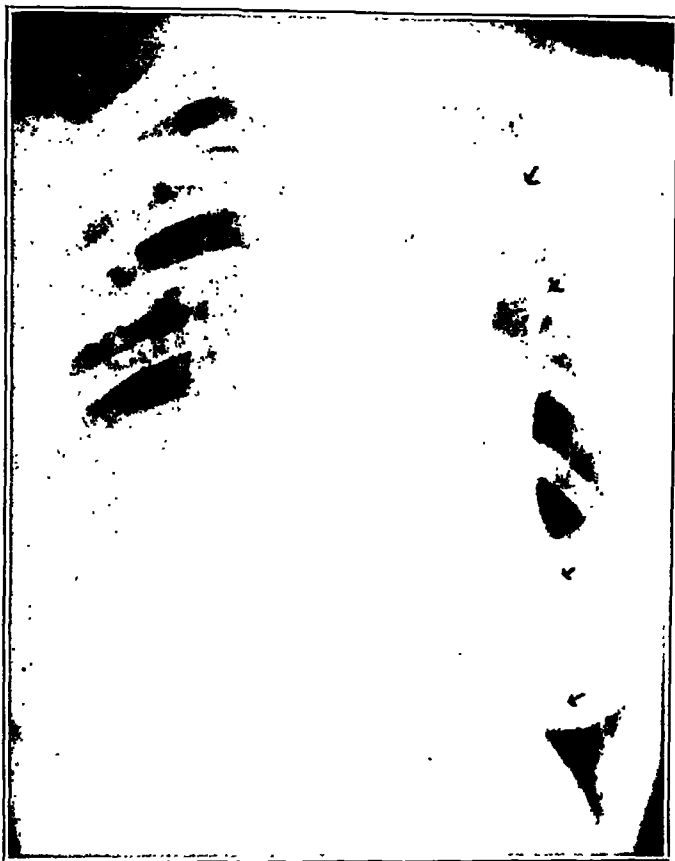


Fig. 10.—Patient shown in figure 9 in inspiration twenty-four hours after introduction of 300 cc. of air.

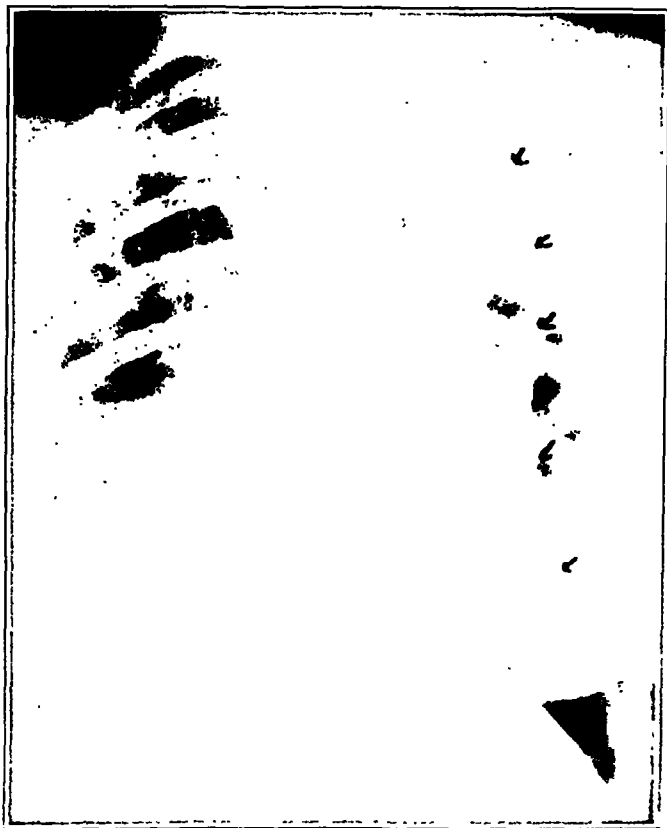


Fig. 11.—Patient shown in figure 9 in expiration twenty-four hours after introduction of 300 cc. of air; the even distribution of gas in the left pleura without change in inspiration or expiration should be noted.

EFFECT OF HIGH INTRAPLEURAL PRESSURES ON PATHOLOGIC
AND ANATOMIC LUNG TISSUE

The difference in consistency between pathologic and normal anatomic lung tissue is another fundamental principle influencing the localization of gas in the pleural cavity. Soft and edematous lung tissue contains little air, and it requires but little compression to render such tissue entirely airless, reducing it to a solid mass, until it reaches the limit beyond which it cannot be compressed any more. The volume

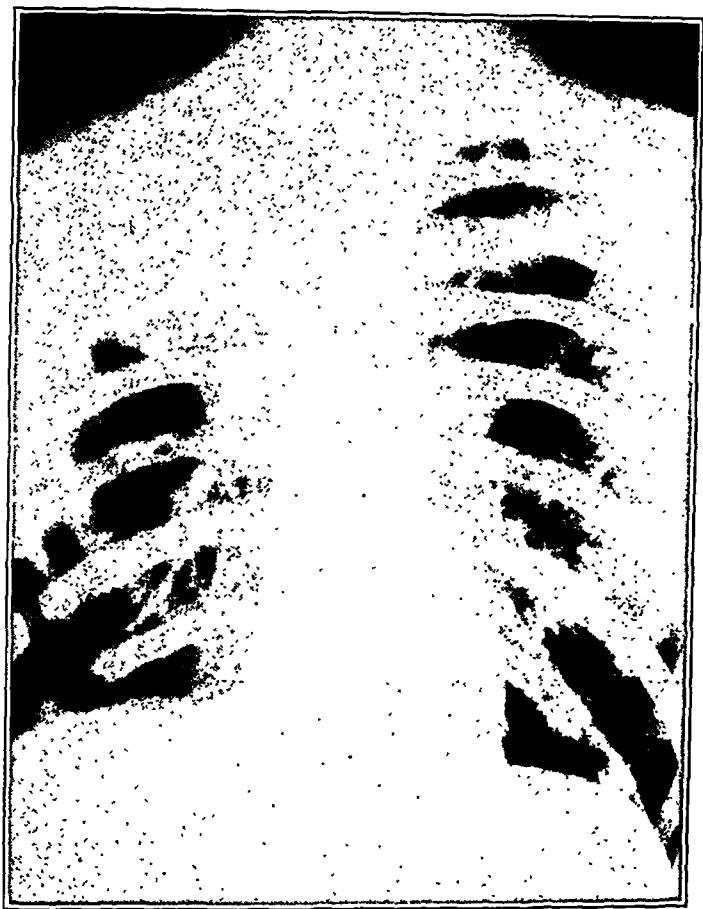


Fig. 12.—Confluent infiltration and cavitation of upper third of right lung.

of functioning lung tissue, like a sponge, consists of a great deal of air enclosed in its alveoli, and therefore when it is rendered into an airless and solid mass by high intrapleural pressure, it is reduced to a much smaller volume than diseased tissue would be under the same force of compression. This is why the older observers of pneumothorax thought erroneously that healthy lung tissue becomes more easily compressed than diseased tissue, because they administered large amounts of air, creating a positive intrapleural pressure, often as high as $+60 + 40$ mercury. Figures 12, 13 and 14 serve as a clear cut illustration in this respect.

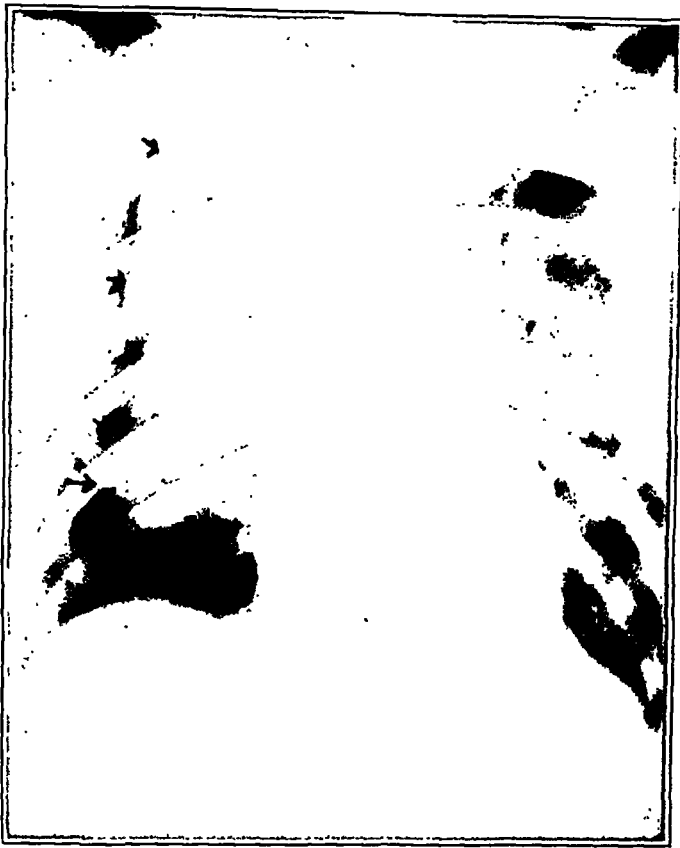


Fig. 13.—Patient shown in figure 12 after development of right spontaneous pneumothorax; intrapleural pressures at this time were $+30 + 70$ mm. water manometer; the lower nondiseased portion of the lung has been reduced to a lesser volume than the upper diseased portion.



Fig. 14.—Patient shown in figures 12 and 13 twenty-one days after the spontaneous pneumothorax; intrapleural pressures were $-40 - 30$ mm. water manometer; there is reexpansion of the lower functioning portion of the lung.

The prepneumothorax roentgenogram is shown in figure 12, revealing a massive confluent infiltration of the upper third of the right lung. If a small amount of air were introduced into this pleural cavity, leaving the intrapleural pressures negative, it should have localized itself over the diseased area, according to the pneumodynamic principles explained previously. However, the diseased portion would soon reach its limit of compressibility, and if a larger amount of air were administered it would naturally affect the nondiseased portion of the lung, com-



Fig. 15.—Patient shown in figures 12, 13 and 14 in inspiration three months later; the upper diseased portion, which is markedly compressed, and the lower functioning portion, which expands to almost full capacity with the respiratory phases, should be noted.

pressing it more the higher the intrapleural pressure created. Figure 13 exemplifies this view. It is a roentgenogram of the same patient as shown in figure 12, taken twenty-four hours after the development of spontaneous pneumothorax. The intrapleural pressures at this time were $+30 + 70$ mm. water manometer. The lower nondiseased portion of the lung has been reduced to a lesser volume than the upper diseased portion of the lung. Twenty-one days later another roentgenogram was

taken (fig. 14) which shows a complete reexpansion of the lower unaffected portion of the lung. The intrapleural pressures at this time were $-60-30$ mm. water manometer. Since then he has been given refills in the amounts of 400 to 500 cc., leaving the intrapleural pressures always negative. Figures 15 and 16 are roentgenograms of the same patient taken three months later in inspiration and expiration, respectively. The upper diseased portion is markedly compressed, showing

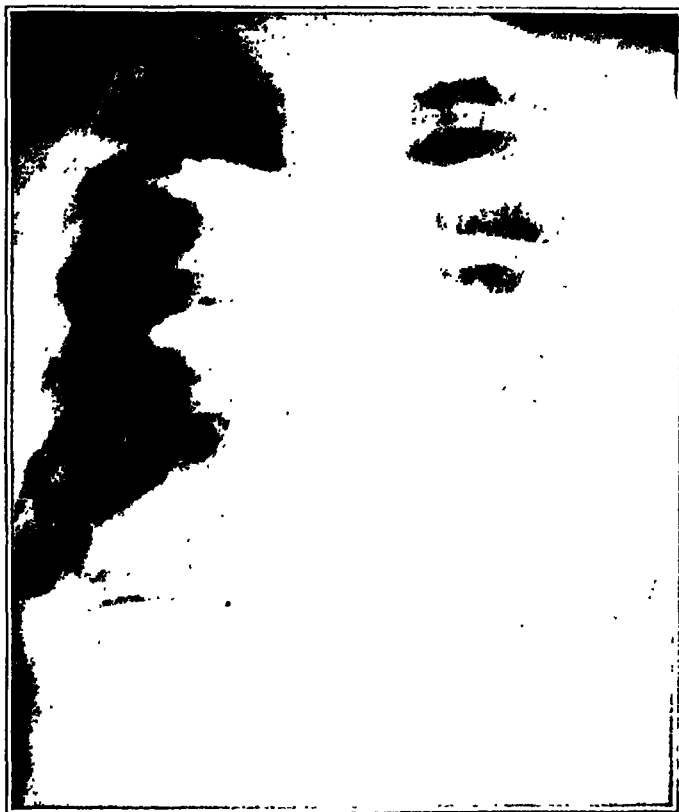


Fig. 16.—Patient shown in figures 12, 13 and 14 in expiration three months later.

little changes with the respiratory phases, whereas the lower non-diseased portion of the lung expands and contracts fully with each inspiration and expiration.

INSUFFLATED AMOUNTS WITH RELATION TO DISEASED AND NONDISEASED PORTION OF LUNG

Barlow and Kramer,² in a remarkable contribution on artificial pneumothorax, have drawn attention to the fact that gas introduced into the pleural cavity will tend to localize over the diseased portion of the lung, and they called this phenomenon "selective collapse." However, it is

2. Barlow, N., and Kramer, D.: Selective Collapse Under Partial Pneumothorax, *Am. Rev. Tuberc.* 6:75 (April) 1922.

obvious enough that the name is only apt to mislead; the gas has no predilection for the diseased tissue but distributes itself according to the existing pneumodynamics. It is the *expansile portion* of the treated lung that is more resisting to low pressures by virtue of the atmospheric pressure to which its intrapulmonary surface is subjected, and this expansile portion drives and keeps the gas over the diseased area. But when the amount of air introduced into the pleural cavity is too large to be contained in the space left by the contracted diseased portion,

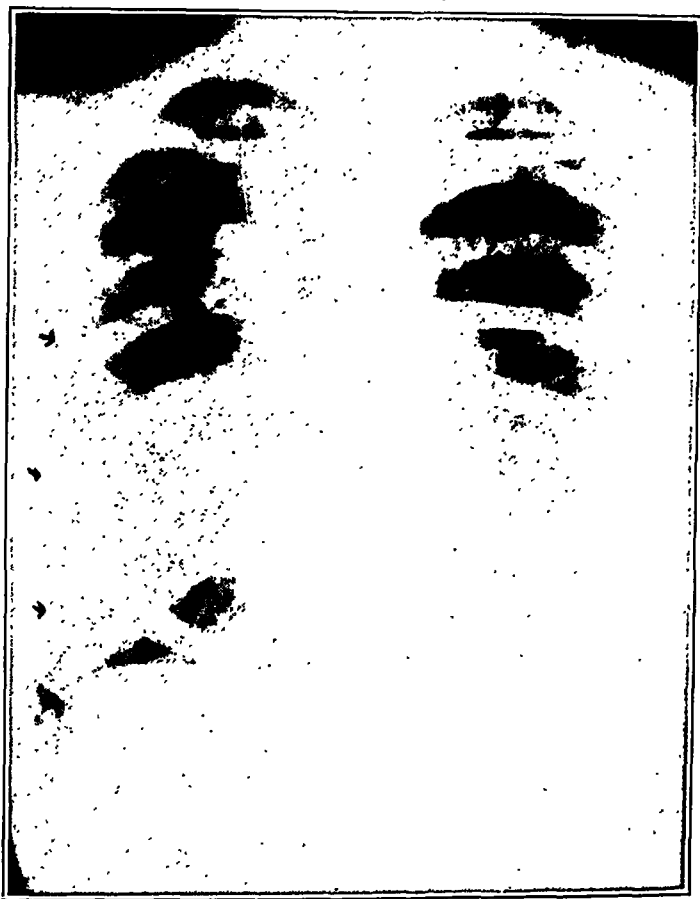


Fig. 17.—Patient shown in figure 1 five months after initiation of pneumothorax; 400 cc. were inflated at this time; there are compression and complete obliteration of cavity of upper lobe, and the lower functioning portion expands to its full capacity pushing its way into space left by the compressed area.

it will naturally encroach also on the functioning portion, and the greater the amounts of gas administered the more will this expansile portion be limited in its function.

Only careful and frequent roentgenoscopic observations will give one a fair idea of the amount to be inflated in order to keep the diseased portion compressed without affecting the functioning portion to a great extent. Figure 17 is a roentgenogram of the same patient as shown in figure 1, taken five months after the initiation of pneumothorax. The amount of air given at the last refill was 400 cc., and the intrapleural

pressures were — 80 — 30 mm. water manometer. From the roentgenogram one can observe that the 400 cc. has occupied wholly the space left by the contracted diseased portion, leaving the lower functioning portion of the lung almost unaffected. At the next reinflation 900 cc. was given, and the effect on the functioning portion of the lung is clearly noticeable in figures 18 and 19. The expansile portion of the lung has been reduced to more than half its size during inspiration and to almost its minimum during expiration, whereas the contracted diseased portion has not been affected at all by this large amount of air



Fig. 18.—Patient shown in figure 17 in inspiration after the inflation of 900 cc.

and high intrapleural pressure. In other words, 400 cc. was enough to keep the diseased part at rest without affecting the nondiseased portion of the same lung; each 100 cc. exceeding these 400 was of no apparent therapeutic value, but curtailed the function of the expansile portion and thereby decreased the vital capacity of the patient, which in turn brought on dyspnea.

Obviously, it is the relation of the insufflatory amounts to the extent of the functioning portion of the lung that determines the localization of the gas. Any undue increase in the amounts inflated fetters also the function of the expansile portion; the greater this functioning portion is the smaller are the amounts to be administered, and vice versa.

Furthermore, in measuring the intrapleural pressures at various levels, I found it much higher over the compressed diseased portion than the expansile portion, in the inspiratory phase only. This means that the functioning portion of the treated lung expanding fully during inspiration leaves the pleural pressure almost at its physiologic negativity, whereas the small amount of air caused to accumulate over the

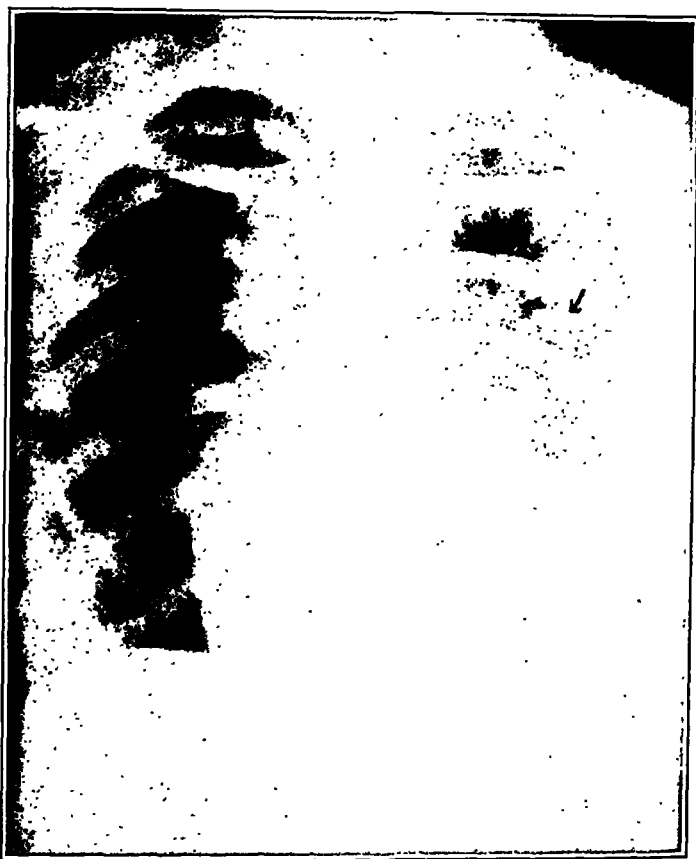


Fig. 19.—Patient shown in figure 17 in expiration, after the inflation of 900 cc. In figures 18 and 19 the reduction of the lower functioning portion to half its size during inspiration and to the minimum during expiration should be noted; the compressed diseased portion was not affected at all; there was marked displacement of the mediastinum.

diseased portion increases the intrapleural pressure at that area. Only by small insufflatory amounts given at frequent intervals can this phenomenon be demonstrated.

CIRCULATORY CHANGES AND COMPENSATORY EMPHYSEMA

The various circulatory changes resulting from the deflation of one lung and the value of observing these changes in regulating the intervals and amounts of gas to be inflated into the pleural cavity, as well as their significance in the prognostication of the case treated, has been

discussed in another article.³ However, I want to emphasize here that the compensatory ability of the right ventricle assists a great deal in keeping the functioning portion expanded and in the production of compensatory emphysema also in the contralateral lung.

The sharp distinction between compensatory emphysema and hypertrophic emphysema should always be borne in mind. In hypertrophic emphysema the pulmonary capillaries are thinned out because of the overdistention of the elastically weak alveolar walls, whereas in compensatory emphysema the distention of the alveoli is a result of the overfilling of the pulmonary capillaries. When the pulmonary capillaries are compressed in one area of the lung, the blood is necessarily diverted to the other pulmonary capillaries, and if the right ventricle compensates well, it drives the same amount of blood *per same unit of time* through a lesser capillary bed, which naturally occasions an overfilling in each pulmonary capillary. This overfilling of the capillaries which surround each alveolus brings about an overdistention of the functioning alveoli.

Yates,⁴ in discussing the existence of an air cell-capillary gear, points out that the air cells and capillaries are not only intimately associated functionally but also closely related physically, and if tortuous capillaries are straightened and elongated by increased unit volumes of blood, the walls of corresponding air cells are carried with them and inflation results. This has been proved experimentally by surrounding a distensible elastic bag with empty rubber tubes and filling these tubes with fluid, which will cause a distention of the elastic bag. By ligating one pulmonary artery in an animal a marked compensatory emphysema in the contralateral lung results. The same has been observed clinically in cases treated with artificial pneumothorax.

The development of compensatory emphysema will take place also in the functioning portion of the treated lung, provided the intrapleural pressure does not exceed the pulmonary intravascular tension, and the more slowly the collapse is produced the easier it is for the right heart to compensate, keeping the pulmonary circulation more competent, which insures a better oxygenation and ventilation of the lung, as can be studied by frequent spirometry.

CHANGES IN VITAL CAPACITY

The vital capacity modifications during the course of artificial pneumothorax treatment are very characteristic, and careful periodic spirometry affords a great deal of information about the respiratory

3. Bendove, R. A.: The Circulatory Changes in Artificial Pneumothorax, *Am. Rev. Tuberc.* **12**:107 (Oct.) 1925.

4. Yates, J. L.: The Significance of Vital Capacity in Intrathoracic Therapy, *Arch. Surg.* **10**:477 (Jan.) 1925.

recuperation of the lungs and how to regulate the insufflatory amounts. In an article on this subject⁵ I discussed lengthily the mechanism and the factors modifying the vital capacity and indicated the clinical and prognostic value in the collapse therapy. Suffice it to mention here that the vital capacity in cases treated with expansile pneumothorax is not reduced much throughout the treatment. There is never a quantitative relation between the amount of air introduced into the pleural cavity and the reduction of the vital capacity. For instance, if the vital capacity is 2,500 cc. before inflation, it will be about 2,300 after the injection of 500 cc. of air into the pleural cavity, i. e., a reduction of only 200 cc. in the vital capacity, though 500 cc. was given. This is explained by the fact that the *residual air* of the functioning portion of the treated lung is expelled with each deep expiration, becoming an integral part of the vital capacity. The participation of the residual air in the vital capacity explains why patients treated with artificial pneumothorax of the expansile type are less dyspneic than other tuberculous patients with the same low vital capacity.

In cases in which the low vital capacity is due not to anatomic extent of the lesion but to severe toxemia caused by this lesion, it might even increase after the establishment of pneumothorax of the expansile type, as it was demonstrated in the following case:

The patient was very dyspneic on admission, had high fever and marked general malaise. The vital capacity was 1,600 cc. Physical and roentgenologic examinations revealed an extensive basal lesion of the exudative type in the right lung. After initiation of pneumothorax therapy the condition remarkably improved. The pneumothorax was of the expansile type. Three months after initiation of pneumothorax therapy, the patient had been practically symptomless and her vital capacity was 2,100, an increase of 500 cc. Frequent roentgenologic observations showed the diseased portion completely compressed, while the upper lobes continued to expand and contract with each respiratory phase. There is no doubt that the low vital capacity prior to the pneumothorax was due to the severe toxemia, but after the abatement of all the toxic symptoms during this therapy, the vital capacity returned to its physiologic point. However, if large amounts of air were introduced compressing also its functioning portion of the treated lung, the vital capacity would have remained greatly reduced.

It is obvious enough that the greater the extent of the expansile portion of the treated lung, the less the vital capacity is reduced, and vice versa.

CLINICAL CONSIDERATIONS

Because of the pneumodynamic principles just discussed, gas introduced into the pleural cavity can be made to localize over the diseased portion of the lung, provided no adhesions exist and the gas is given in the proper amounts. It is to be remembered that we administer gas

5. Bendove, R. A.: The Vital Capacity in Artificial Pneumothorax, Arch. Int. Med. 36:94 (July) 1925.

not with the purpose of compressing the *entire* lung, but to keep the *diseased portion* alone at rest. It is out of the scope of this article to go into a discussion whether the benefit of pneumothorax therapy is due only to the rest of the diseased lung or also to certain immunologic reactions that might follow the collapse. This has been discussed fully in another article⁶ and a theory was advanced to explain why healing at times takes place by resolution instead of fibrosis in cases treated with the expansile type of pneumothorax.

However, it is to be emphasized that it is possible to keep the diseased portion compressed without curtailing all the function of the uninvolved part of the same lung. Of course, when the entire lung is affected no expansile type of pneumothorax can be expected, but when only a portion of the lung is involved the expansile type of pneumothorax is the treatment of choice.

The amount of air to be given at initial inflation should never exceed one-seventh the vital capacity of the patient; the subsequent refills should be guided not only by the vital capacity but also by the principles of gas localization outlined above. No generalization as to the amount of air to be given can therefore be made, but each case should be individualized, depending on the extent of the involved and uninvolved portions of the treated lung. These can be accurately studied only by frequent roentgenoscopic examinations.

Furthermore, the insufflatory amounts and the intervals at which they are to be given differ often even in the same person. Frequent physical examinations, roentgenoscopic observations, spirometry and careful study of the circulatory changes are the best criteria how to modify the refills. The amounts may vary from 200 to 400 cc., and the intervals from five to ten days the first few months. It is to be remembered always that the gas is given with the purpose of keeping the diseased portion alone compressed, and only by frequent refills in small amounts can the gas localization be brought about.

The patients successfully treated with the expansile type of pneumothorax are usually young persons with a soft or exudative type of lesion of not very long duration, the pleura of which is free from adhesions. Such patients usually have a good cardiac reserve and the elasticity of their lungs is at its best, leading to a development of compensatory emphysema which assists in better ventilation of the lung, preventing undue dyspnea.

Complications, particularly pleural effusions, seem to be much less frequent in cases treated with this type of artificial pneumothorax. However, no definite statement can as yet be made in this respect. Further observations are necessary.

6. Bendove, R. A.: Resolution and Healing in Pulmonary Tuberculosis, *M. J. & Record* **121**:36 (Jan. 7) 1925.

THORACOPLASTY VERSUS ARTIFICIAL PNEUMOTHORAX OF
THE EXPANSILE TYPE

It is not the purpose of this article to go into details of the comparative advantages and disadvantages of artificial pneumothorax and thoracoplasty. Alexander⁷ has gone into this question carefully in his book on thoracic surgery in pulmonary tuberculosis, to which the reader is referred. However, Alexander failed to consider the fact that artificial pneumothorax per se is not as yet a standardized method, but may itself be divided into several types, each of which has a different action on the treated lung. In my article on the classification of artificial pneumothorax and the clinical value of the several types¹ I said: "statistics on the result of artificial pneumothorax, so far collected, have little value because the kind of pneumothorax used in each case was never taken into consideration, and thus altogether unequal elements were being compared, inasmuch as the various pneumothoraces acted on normal and pathological lung tissue in mechanically and physiologically different ways."

Furthermore, in evaluating the mode of action and results of treatment of either pneumothorax or thoracoplasty, we must take into consideration the type of pulmonary tuberculosis on which these methods were used. The difference between the productive or proliferative types and the soft caseous or exudative types of tuberculosis should always be kept in mind. The soft caseous lesion or the exudative type represent a condition in which the body shows little reaction in the way of defense and the process of destruction preponderates over the process of repair in the pulmonary tissue, whereas the proliferative or productive type indicates a preponderance of granulation tissue which is being produced at the site of the lesion. This division is an anatomic-pathologic differentiation, but it denotes a definite clinical differentiation: the proliferative variety usually is chronic in type and may exist for many years without any clinical manifestation, whereas the exudative variety usually is of the acute or subacute type and gives rise to symptoms early in its development.

It is in the proliferative type of pulmonary tuberculosis that thoracoplasty is to be resorted to, as when such patients begin to show symptoms the lesion is usually far advanced with marked pleuritic adhesions rendering pneumothorax unavailable. The exudative type of pulmonary tuberculosis, on the other hand, will benefit little by thoracoplasty, because the latter never compresses the diseased part fully and the stimulation to fibrous tissue formation is not very successful in such cases. As was indicated above, such types of pulmonary disease

7. Alexander, J.: *Surgery of Pulmonary Tuberculosis*. Philadelphia: Lea Febiger, 1925.

culosis usually manifest themselves clinically early in their evolution, in their first or second stage of anatomic involvement, and the treatment of choice is the expansile type of pneumothorax, which effects a complete compression of the diseased portion without reducing very much the function of the nondiseased portion of the treated lung.

A comparison of figures 1 and 17, two roentgenograms of the same patient, one taken prior to initiation of pneumothorax and the other taken five months later, shows the remarkable result obtained by the expansile type of pneumothorax. The cavity has become obliterated and the entire lesion has been compressed and reduced to its minimum. The same results were obtained in the basal lesions, as seen from comparison of figures 5 and 8. This could never have been accomplished by thoracoplasty, even if the entire length of the ribs was removed. Furthermore, the nondiseased portion of the treated lung was affected only slightly, its ventilatory function becoming at times even more efficient, as was discussed fully in considering the circulatory changes and the vital capacity.

Thoracoplasty has been considered as the ultimum refugium treatment in pulmonary tuberculosis; still the modern thoracic surgeon hopes—and perhaps rightly so—"that the specialists in tuberculosis will soon refer for surgery many patients whose disease is far less advanced than are those who are at present being operated upon,"⁷ and any one will endorse the following statement of Graham⁸ in regard to thoracic surgery:

In the future it will unquestionably be made safer by better understanding of the physiology and pathology involved, by a more precise drawing of operative indication, and by a closer cooperation between the internists and surgeons, which will permit the carrying out of operative procedures at a time when they may prove of real benefit with a minimum risk instead of being last resorts in patients who are already nearly dead.

Artificial pneumothorax, rightly belonging to the domain of thoracic surgery, though because of the long period of time its application requires it is considered as a "medical" treatment, is still looked on by many as a last resort measure in the treatment of pulmonary tuberculosis. In view of this newer understanding of the mechanism and effect on the diseased and nondiseased lung tissue, pneumothorax, particularly of the expansile type, should be recognized as the treatment of choice in the exudative type of pulmonary tuberculosis, and is to be administered as early as possible. It throws little burden on the respiratory function of the contralateral lung; it effects complete compression of the diseased portion without curtailing the function of the nondiseased portion of the treated lung; it makes little demand on the

8. Graham, E. A.: Recent Phases of Thoracic Surgery, *J. A. M. A.* 80:1-25 (June 23) 1923.

cardiac reserve; it reduces the vital capacity but little, if any, and the gradual development of compensatory emphysema in the functioning portion of the treated lung replaces and fills the hemothorax gradually without causing any deformity. A slight or even moderate involvement of the contralateral lung is not a contraindication for this therapy, because in this type of pneumothorax little extra demand, if any, is made on the respiratory function of the other lung.

CONCLUSIONS

The difference in the elasticity of the diseased and nondiseased lung tissue as well as the difference in the intrapulmonary and intrapleural pressures make it possible for the introduced gas into the pleural cavity to localize itself over the diseased portion without curtailing much of the function of the unaffected portion of the treated lung, provided the amounts administered are small and are given at frequent intervals. These pneumodynamic principles should be made use of in every case treated with artificial pneumothorax; they are best applied, however, in cases of the exudative type of pulmonary tuberculosis of not very long duration which are free from pleural adhesions. In such cases pneumothorax therapy is not to be considered as a last resort measure, but as the treatment of choice, as it offers a more speedy and more complete anatomic and functional recovery.

These pneumodynamic principles of gas localization cannot, as a rule, be applied in cases of the productive or proliferative type of pulmonary tuberculosis, because such cases usually run a mild clinical course, and when they begin to manifest severe symptoms they are usually far advanced and marked pleuritic adhesions are present, rendering a therapeutic pneumothorax inapplicable. In such cases thoracoplasty is the indicated treatment provided the contralateral lung is in good condition.

A slight or even a moderate involvement of the other lung is not a contraindication for artificial pneumothorax of the expansile type, because the function of the undiseased portion of the treated lung is not curtailed much, and little demand is made for extra respiratory function on the other lung. The insufflatory amounts in such cases should vary from 200 to 400 cc. of air and the intervals from five to ten days. No generalization can be made, but each case is to be individualized, depending on its vital capacity and extent of involved and uninvolved portions of the treated lung. This can be studied only by frequent roentgenoscopic observations and periodic spirometry.

INVOLUTIONAL OR REGRESSIVE CHANGES IN THE THYROID GLAND IN CASES OF EXOPHTHALMIC GOITER

AND THEIR RELATION TO THE ORIGIN OF CERTAIN OF
THE SO-CALLED ADENOMAS *

WILLIAM FRANCIS RIENHOFF, JR., M.D.

BALTIMORE

INTRODUCTION

Nearly a century has now passed since Robert Graves¹ in 1835 first described the clinical syndrome that at present bears his name and characterized this disease as being due to an hypertrophy of the thyroid gland. The first descriptions of the histologic changes occurring in hypertrophy and hyperplasia of the thyroid gland were made in 1886 by Horsley² and in 1896 by Halsted,³ when they reported the compensatory changes occurring after partial thyroidectomy in animals. Greenfield⁴ in 1893 expressed the belief that certain specific changes occurred in the structure of the thyroid gland in exophthalmic goiter and this has been confirmed by many observers, most notable among whom are Lewis,⁵ MacCallum,⁶ Hanseman,⁷ Lubarsch,⁸ Ewing,⁹ Wilson,¹⁰ MacCarty¹¹ and Kocher.¹²

The studies made by these observers have been so detailed and complete that little new has been added to this subject in recent years, and the histologic changes occurring when the thyroid gland undergoes hypertrophy and hyperplasia, whatever the degree, are today fairly well

* From the Department of Surgery of Johns Hopkins University.

1. Graves, Robert: Clinical Lectures, 1835, Philadelphia, Adam Waldie, 1838.

2. Horsley, Victor: Brown Lectures, *Lancet* 2:1163 (Dec. 19) 1886.

3. Halsted, W. S.: An Experimental Study of the Thyroid Gland in Dogs with Special Consideration of Hypertrophy of the Gland, *Johns Hopkins Hosp. Rep.*, 1896, p. 373.

4. Greenfield, W. S.: Some Diseases of the Thyroid Gland, *Brit. M. J.*, 1893.

5. Lewis, Dean: The Pathological Anatomy of Exophthalmic Goiter, *Surg. Gynec. Obst.* 3:476, 1906.

6. MacCallum, W. G.: Pathology of Exophthalmic Goiter, *J. A. M. A.* 49:1158-1162 (Oct. 5) 1907.

7. Hanseman: *Berl. klin. Wchnschr.*, Oct. 30, 1905.

8. Lubarsch: Schilddrüsenveränderung bei Basedowischer Krankheit, *Centralbl. f. allg. Pathol. u. path. Anat.* 6:716, 1895.

9. Ewing: *Tr. A. Am. Phys.* 21:567, 1906.

10. Wilson, L. B.: *Am. J. M. Sc.*, December, 1908.

11. MacCarty, W. C.: *Mayo Clinic Papers*, 13, 1912.

12. Kocher, Albert: *Arch. f. path. Anat.* 208:86; 161, 1912.

understood. It is now a well recognized fact that there exists, clinically, different degrees of hyperthyroidism, from the most mild to the most severe; the latter syndrome usually comes under the classification of exophthalmic goiter. The clinical course of the cases of exophthalmic goiter also varies to a great extent; for instance, the most severe or fulminating cases have, as a rule, a relatively acute onset followed by a short, unremitting course of the disease which, if allowed

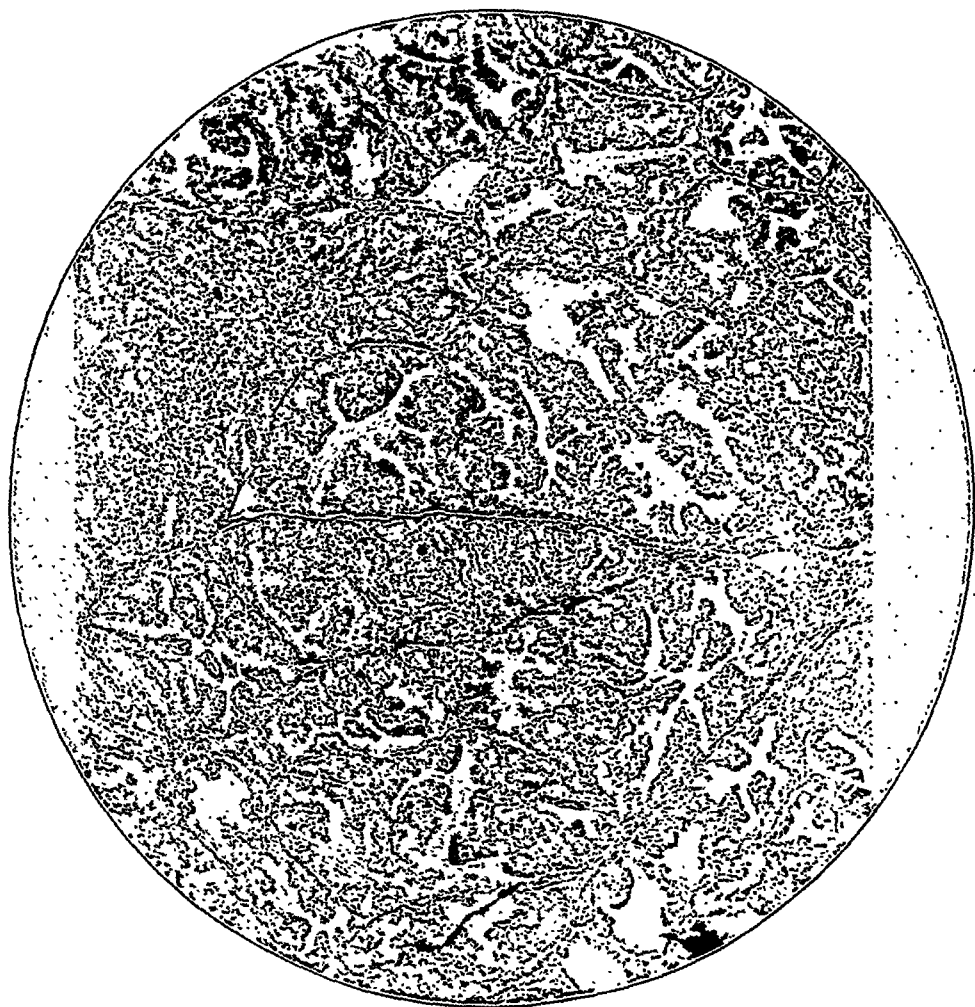


Fig. 1 (case 1).—One of a series of sections of excised right lobe before involution or administration of iodine, under low power (40 mm. lens); classical histologic structure of extreme hypertrophy and hyperplasia seen in a typical case of exophthalmic goiter; marked increase in parenchyma and decrease in colloid spaces; fibrous tissue increase plain in lobulation of gland; some lobules made up entirely of small acini.

to progress untreated, ends in death in a large percentage of the cases. In the less severe cases the clinical course consumes a great deal more time and is attended with one or more remissions and exacerbations even though it remains untreated throughout its course.

In the more mild cases of hyperthyroidism not severe enough to be classified as exophthalmic goiter the occurrence of remissions and exacerbations is of still greater frequency. In all instances of hypertrophy and hyperplasia of the thyroid gland whether pathologic or physiologic, remissions and exacerbations occur, with the exception of the acute fulminating cases of exophthalmic goiter mentioned above, in which remissions do not occur. In general there is a definite parallelism



Fig. 2 (case 1).—Figure 1 under higher magnification ($\times 170$); dilated vessels, lymph and blood in stroma, very active hypertrophy and hyperplasia of epithelium readily seen; acini empty except for clear, nonstaining vacuoles, mottling of epithelium and vesicular character of nuclei are evident; epithelium thrown up in folds like papillomas; colloid not abutting on epithelium.

between the severity of the clinical course and the histologic changes observed, although in some clinically typical cases the microscopic picture of the thyroid gland is a source of great surprise and subject to the most extensive variations. The result is that many different classifications

have been made for the various microscopic alterations observed but these, up to the present time, have been without a great deal of significance.

In the past a detailed study has been made of the changes in the histologic structure of the thyroid gland resulting from all degrees of hypertrophy and hyperplasia, from the most simple type observed in

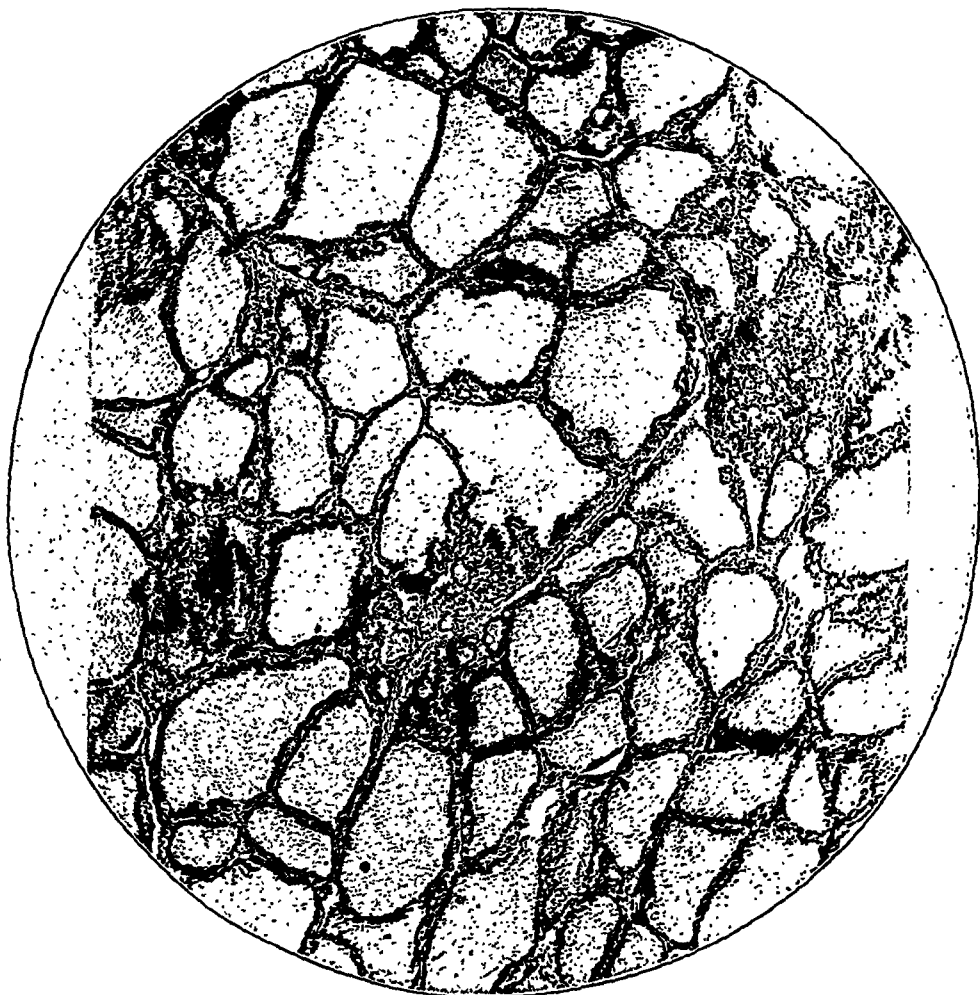


Fig. 3 (case 1).—Typical section of series made of entire gland of case 1 (40 mm. lens) after administration of iodine for three weeks; striking contrast to figure 1 is seen although from same patient; colloid spaces are in great predominance over strikingly decreased amount of parenchyma; this represents the average degree of involution occurring in the gland of this patient.

puberty and compensatory hypertrophy to that occurring in the most extreme hypertrophy and hyperplasia of exophthalmic goiter. However, the changes in the histologic structure of the thyroid gland during a clinical remission or resulting from involution of the gland have not

been considered at all in the human being, and only slightly in animals.¹³ The reasons for this are quite obvious, for until recent years there has been no method at hand which enabled an examiner to decide whether a patient was beginning an exacerbation or a remission. The personal equation entering into the clinical interpretation varied far too much for any dependence to be put in this method of classification. It is now



Fig. 4 (case 1).—Figure 3 after administration of iodine, under higher magnification (176 mm. lens): acini more regular in shape although some in folds of infolding epithelium still persist; acini flattened out from increased amount of colloid; epithelium in figure 4 as compared with figure 2 shows marked flattening in figure 4; acini completely filled with evenly stained colloid throughout, which abuts on epithelium; small areas of persistent hyperplasia seen in figures 3 and 4; nuclei pyknotic.

13. De Ligneris, quoted by Kocher, T.: *Brit. M. J.* **1**, 1901. Marine, D., and Williams, W. W.: The Relation of Iodine to the Structure of the Thyroid Gland. *Arch. Int. Med.* **1**:349-384 (May) 1908. Helwig, Alexander: Zur Postoperative Kropf prophylaxe (Histologie der Hunde-Kanarienvogel-Thyreoidea nach Iod-Entziehung), *Arch. f. klin. Chir. Kongressband* **126**.

recognized that the determination of the basal metabolic rate over a period of time of sufficient length affords an excellent index of the activity of the thyroid gland so that at present a method is available which makes possible the approximate standardization and registration of the degree and amount of hyperactivity or hypo-activity of the thyroid gland. This not only eliminates the error of personal equation of the examining clinician but also on the part of the patient. Again, a spon-

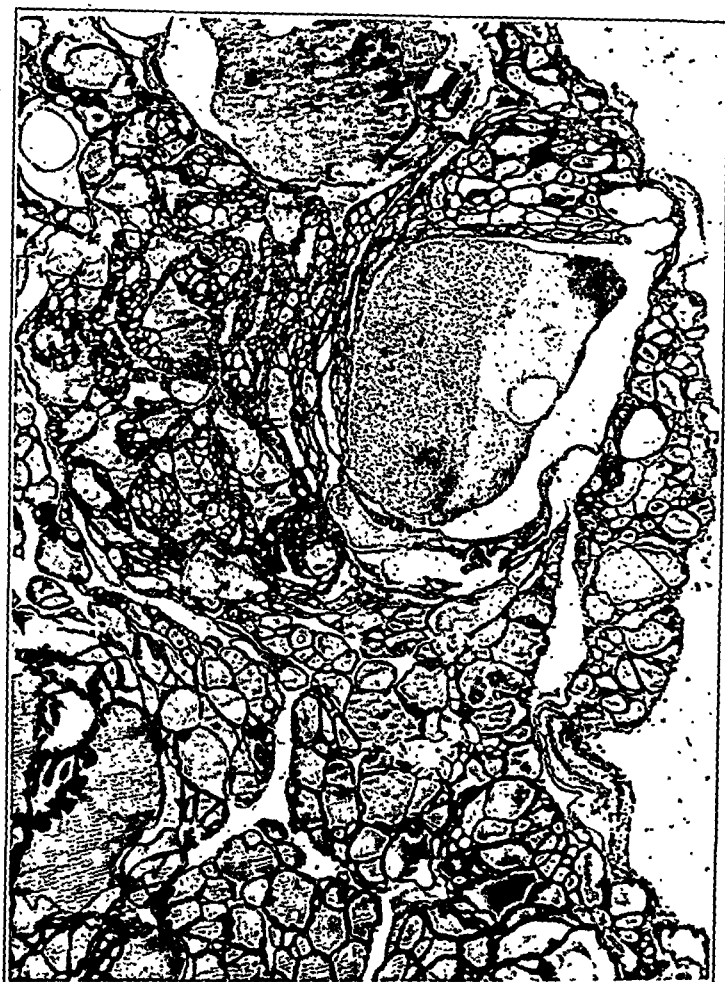


Fig. 5 (case 1).—Large section of gland of patient 1 showing areas of hyperinvolvement, under very low power ($\times 16$); these areas are confined to a lobule compressing the parenchyma in the periphery of the lobule; the areas resemble colloid cysts and colloid adenomas; none of these areas were present in any sections of the gland previous to the involution as a result of the administration of iodine; the involution of the gland about these areas was of average degree for the gland as a whole.

taneous remission as a rule occupies a long period of time and when completed approximates to a greater or less degree the physiologic status of a normal individual and the histologic structure of a normal thyroid gland. So that an examination of the histologic structure of

the thyroid gland at any one point during a remission does not offer an opportunity to study the microscopic changes that have occurred in that gland concomitant with the clinical remission. This is due, of course, to a lack of knowledge of the microscopic appearance of the thyroid gland before the onset of the remission. Mainly for these reasons, it has been impossible in the past to note the microscopic alterations in the thyroid gland due to the changes of involution. With the reintroduction of

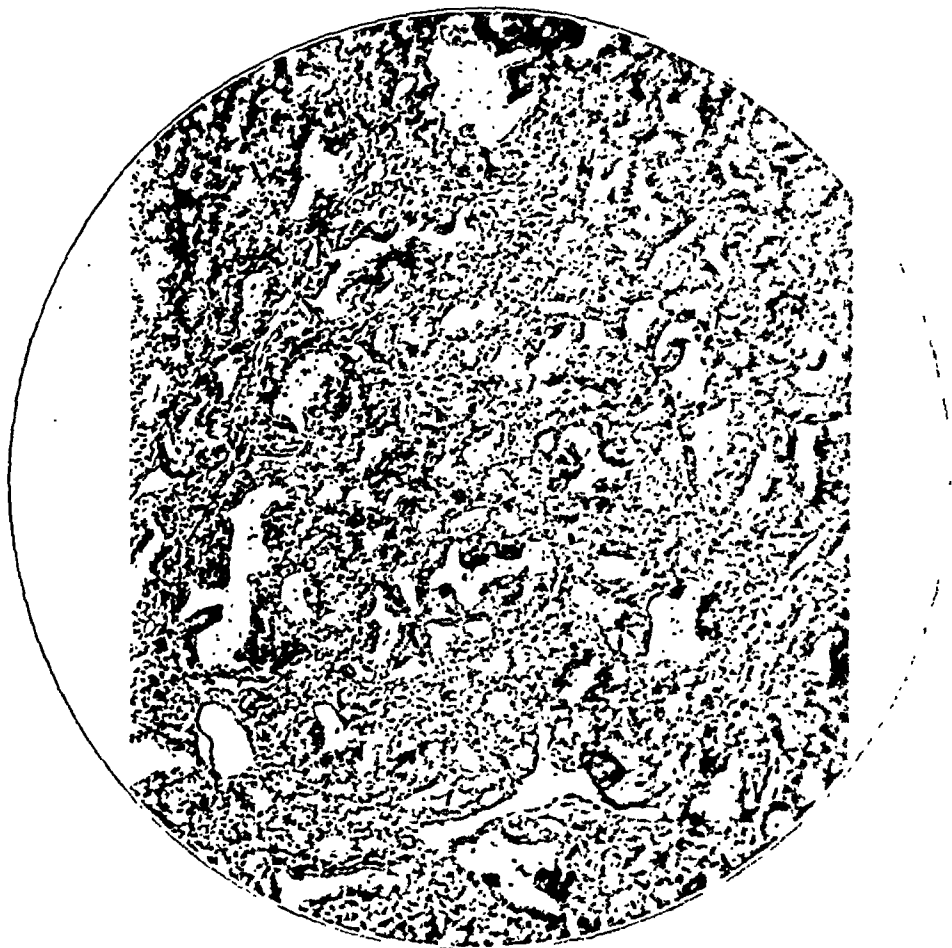


Fig. 6 (case 2).—Gland before involution or administration of iodine (p. 401), typical section of series of upper portion of right lobe including right upper pole, typical exophthalmic hypertrophy and hyperplasia.

iodine in the treatment of exophthalmic goiter a method of producing a precipitous clinical remission was obtained. The most acute and fulminating cases of exophthalmic goiter could be transformed in a period of from two to six weeks into a clinical condition which, in many cases, approximated normal or, at least, a state of a very low grade of hyperthyroidism. This observation has been made many times and

reported.¹⁴ By means of standard doses of iodine, together with the control of the period of time over which it was given, with frequent determinations of the basal metabolic rate, one was enabled to divide the clinical remissions into different periods of completion.

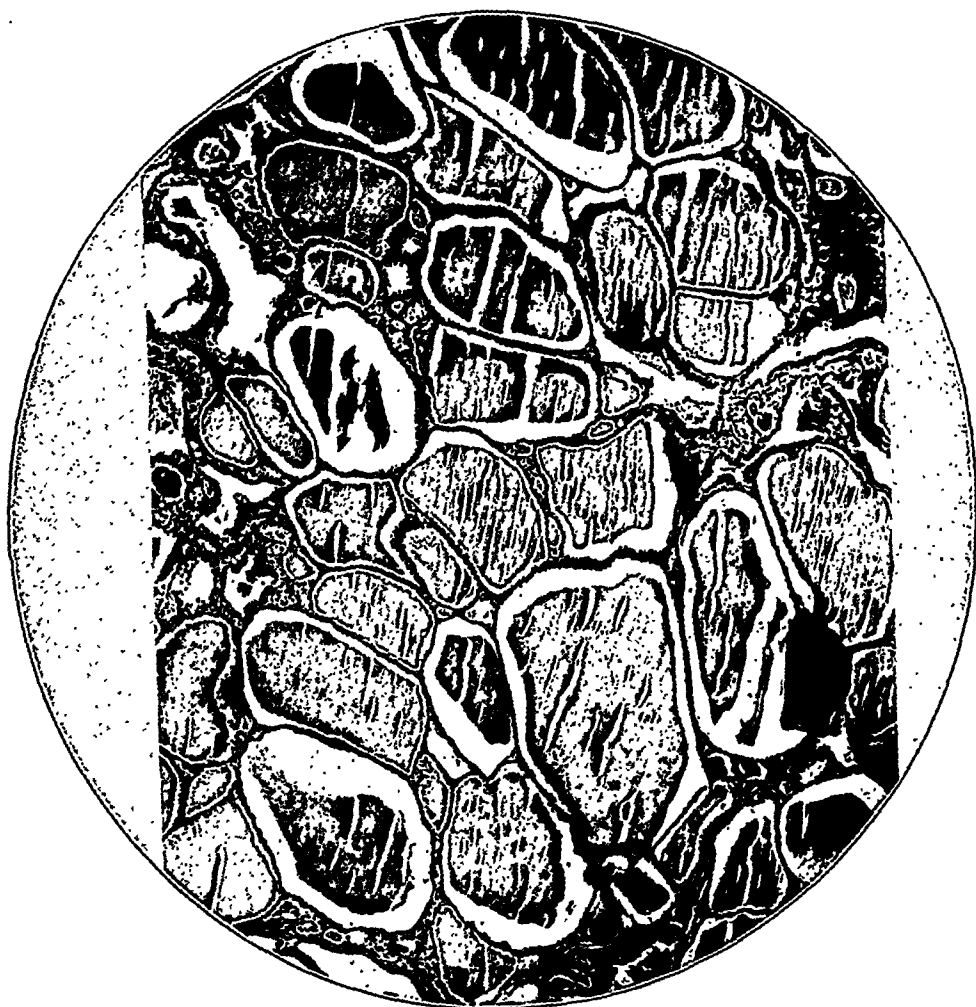


Fig. 7 (case 2).—Section after involution had occurred from iodine administration ($\times 40$); comparison should be made with figure 6; this figure represents the average degree of involution for this case, seen in the gland as a whole; some asymmetry of the acini; interacinous stroma quite delicate and epithelium much flattened so that nuclei stand out on stroma; evenly stained colloid completely filling acini; no vacuoles.

14. Plummer, H. S., and Boothby, W. M.: The Value of Iodine in Exophthalmic Goiter, *J. Iowa S. M. Soc.* 14:66 (Feb.) 1924. Starr, P.; Wolcott, H. P., and Means, J. H.: The Effect of Iodine in Exophthalmic Goiter, *Arch. Int. Med.* 34:355-364 (Sept.) 1924. Thomas, H. M., and Rienhoff, W. F., Jr.: Iodine in the Treatment of Hyperthyroidism, *South. M. J.* 19:87 (Feb.) 1926. Rienhoff, W. F., Jr.: Histological Changes Brought About in Cases of Exophthalmic Goiter by Administration of Iodine, *Bull. Johns Hopkins Hosp.* 37:285 (Nov.) 1925.

METHOD

To determine the changes occurring in the histologic structure of the thyroid gland which accompanied a clinical remission an examination of the microscopic structure of the thyroid gland before the onset of the remission was made. This was accomplished by selecting a series of seven cases of acute fulminating exophthalmic goiter of short duration in which no spontaneous remission had occurred and also in which no form of iodine or treatment of any type had been administered. These

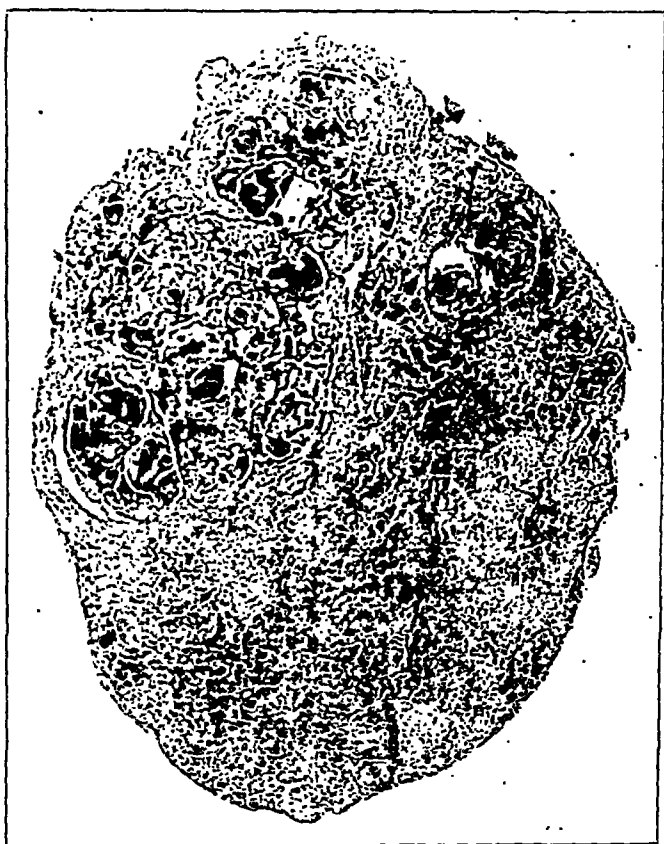


Fig. 8 (case 2).—Section across entire lobe of patient 2 under very low power ($\times 16$) after involution to show asymmetrically placed hyperinvoluted areas that occurred in gland during involution; these resemble colloid adenomas, histologically, the remainder of the gland around these areas undergoing the average amount of involution; no such areas were present in large portion of gland removed before iodine administration.

cases were also selected from a larger group because, following the administration of iodine in each, there was established a typical artificial clinical remission to a condition closely approximating normal. In each of these cases careful clinical and laboratory examinations on admission, including two basal metabolic rate estimations, revealed the fact that

they all presented a clinical picture of a typical case of extreme exophthalmic goiter with their basal metabolic rates varying from 60 to 80 per cent above normal. It is not thought necessary to describe the clinical signs and symptoms of this series except to state that the thyroid gland in each seemed to be increased two or three times in size above normal, was soft and vascular, thrills and bruits occurring at all four poles.

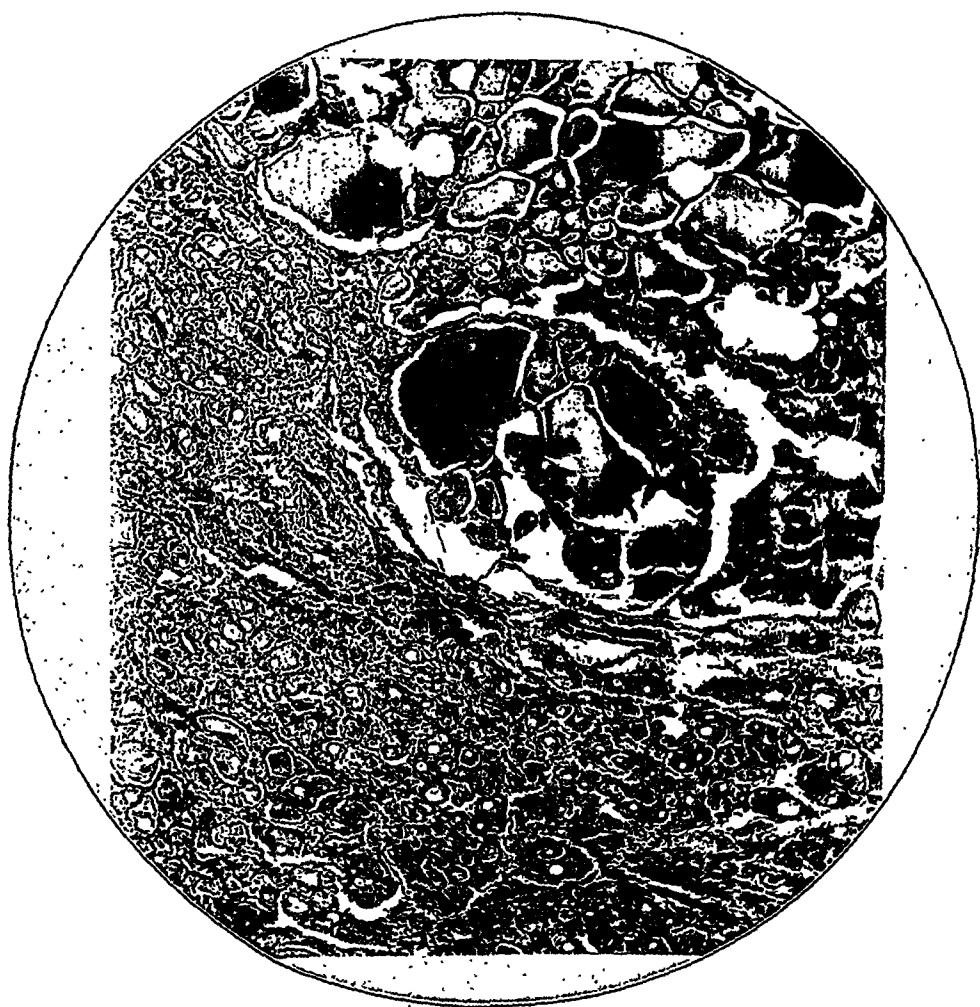


Fig. 9 (case 2).—Figure 8 under higher power ($\times 40$) showing histologic details of hyperinvolved areas; compression of tissue at periphery; localized and encapsulated dilated colloid acini; same microscopic picture observed in many areas of the gland after involution; the gland in the adjacent regions is undergoing the average amount of involution.

The glands were diffusely enlarged throughout and in them no nodules of any size could be palpated.¹⁵ Under local anesthesia a large portion of the entire right lobe including all of the right upper pole of the thyroid

15. A preliminary report of this study was published in *Bull. Johns Hopkins Hosp.* 37:285 (Nov.) 1925.

gland was excised before treatment was instituted. This portion of the gland was then fixed immediately at the operating table in different fixatives, namely, Zenker's solution with 10 per cent formaldehyde, Zenker's solution, Bensley's acetic-osmic bichromate solution containing osmic acid solution, 2 per cent, glacial acetic acid, 1 grain, and potassium bichromate solution, 2.5 per cent. Large and representative serial

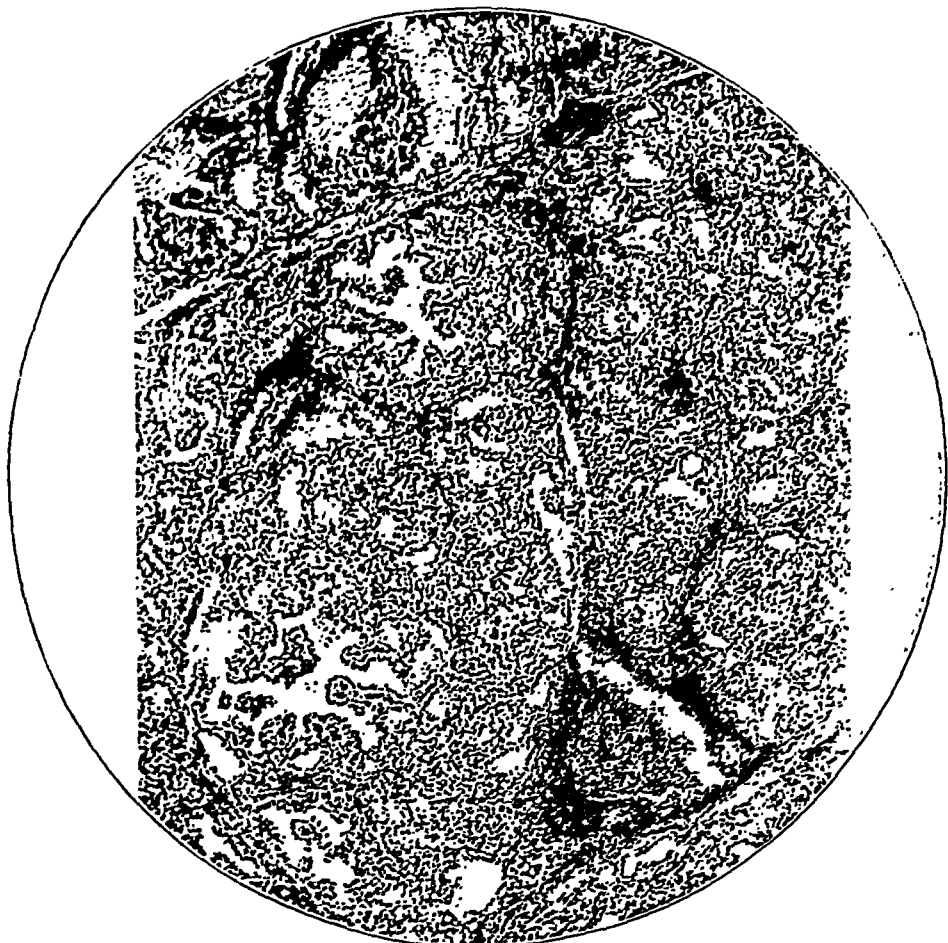


Fig. 10 (case 3).—Typical picture of exophthalmic hypertrophy ($\times 40$); lymphocytic infiltration, absence of colloid, and characteristic section of large portion of right lobe excised before administration of iodine should be noted.

sections were obtained from this excised portion by cutting them transversely across the entire block of tissue. The sections varied in thickness from five to ten microns. The circulation through the remainder of the thyroid gland was disturbed as little as possible. In this manner a careful and detailed study was made of the microscopic appearance and the histologic structure of the thyroid gland in an acute case of exophthalmic goiter at the height of the disease and before any treatment was administered. These patients were then given a com-

pound solution of iodine (10 minims) four times a day, for periods varying from two to four weeks and observed continuously during the administration of the iodine. The estimation of the basal metabolic rates were recorded frequently, every five days. In all cases a definite clinical remission was established, the patient improving remarkably, and the basal metabolic rates fell well below 20 per cent above normal.

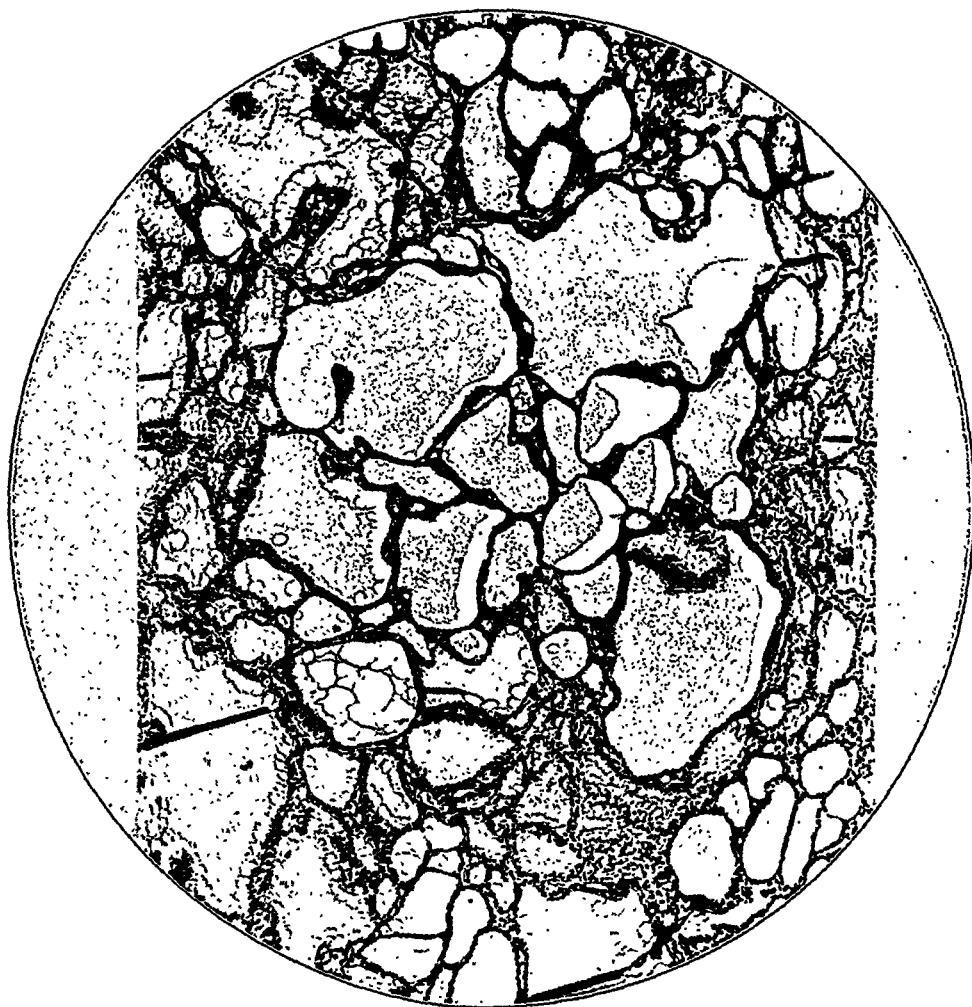


Fig 11 (case 3).—Typical amount of involution occurring in gland as a whole after administration of iodine ($\times 40$); slightly more than usual vacuolization; some infolding of epithelium; according to Aschoff's and Kocher's terminology, this would be called either *struma diffusa colloides macro follicularis proliferans* or *struma colloides Basedowiana*; some acini are larger than others and distention of these has thinned the walls. Comparison should be made with figures 10 and 11.

Operation was then performed on these patients, at which time a double partial lobectomy of the thyroid gland was done. These specimens were immediately fixed as above noted and again serial sections were cut from all portions of the gland removed. Thus, an opportunity was afforded

to compare the histologic changes in the thyroid gland observed at the height of the disease with the microscopic alterations occurring in the gland concomitant with a clinical remission. As the histologic structure of the several glands of this series showed the same alterations and changes before and after the remission and involution, they will be described collectively as a group of cases rather than individually, thus obviating needless repetition. In order to demonstrate the full extent

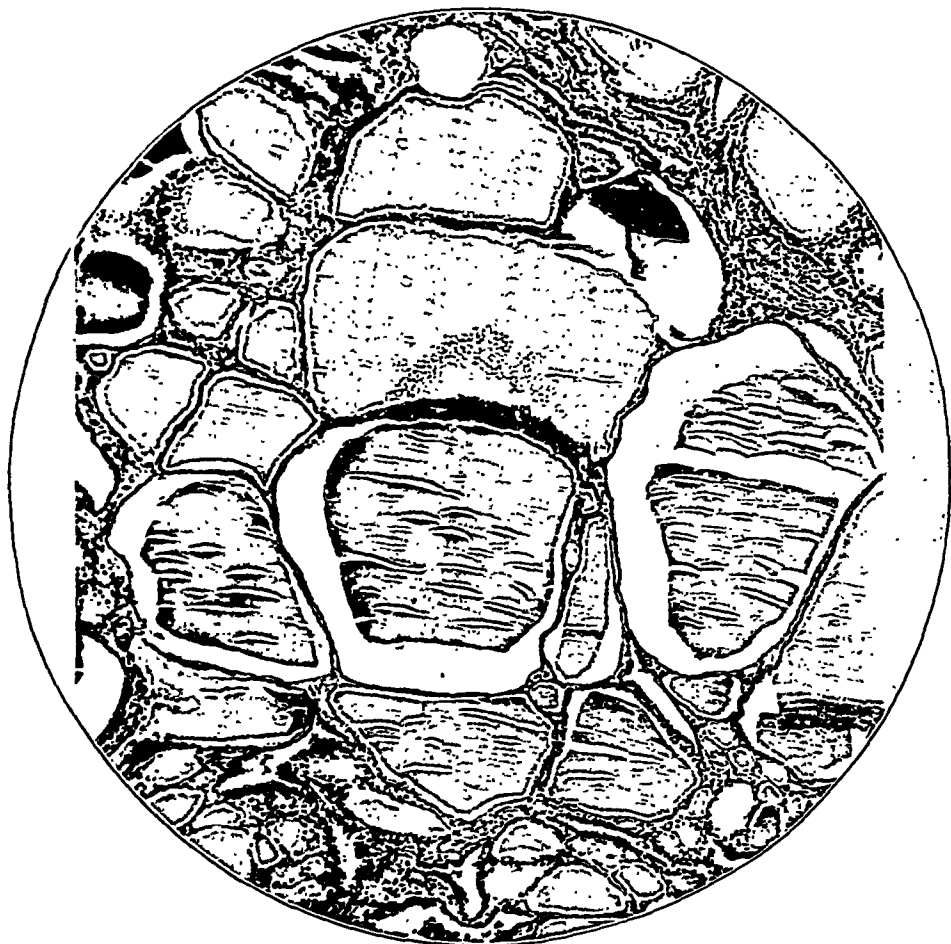


Fig. 12 (case 3).—Gland after involution of iodine ($\times 80$); area of hyperinvolution that is beginning to be demarcated from the rest of the gland by involuting more completely than the average amount throughout the gland; comparison should be made with figure 10; vacuolization of the colloid at one point opposite one side of the middle acinus where there is proliferation of the epithelium on the one side only seems to bear out Aschoff's idea of there being a germinal center in each follicle which is the center from which new acini develop; however, in the light of figure 10 we know that this stage is less active, histologically and clinically, and instead of being, as one would suppose if only this section were obtained without a previous standard for comparison, a point of beginning proliferation it is one of the last dying embers of proliferation.

of the histologic transformations during the involution, and also to show the microscopic appearance of the type of thyroid gland existing in this series before the involution occurred, a full description of the hypertrophy and the hyperplasia occurring in the thyroid glands of these cases is given.

GROSS AND MICROSCOPIC APPEARANCE OF THE THYROID GLAND
AT THE HEIGHT OF THE DISEASE BEFORE THE INVOLU-
TION ESTABLISHED BY THE ADMINIS-
TRATION OF IODINE

Gross Appearance.—The tissue was soft and elastic, very vacular and had the typical raw beef appearance so often observed in exophthalmic goiter. On palpation it imparted a characteristic gland like feel, entirely devoid of any areas of increased or decreased density. The cut surface was coarsely and finely lobulated and somewhat granular in appearance. As a whole, the tissue was of uniform opacity and little or no colloid could be observed.

Microscopic Appearance.—Everywhere the gland was divided into lobules by a fibrous tissue stroma that was definitely increased above normal although relatively delicate. This stroma divided the lobes into lobules which in turn were redivided by the intralobular septums, the latter surrounding completely the follicles or acini. Occasionally large bands of scar tissue traversed the gland, regardless of its lobulation. Throughout the interlobular and intralobular stroma many dilated blood and lymphatic vessels occurred which were distinguished mainly by the contents of the former. The most striking characteristic of the microscopic picture of exophthalmic goiter is well shown in figures 1, 2, 6 and 10; namely, the marked predominance of the parenchyma and the equally pronounced diminution of the colloid. There seem to be two types of hypertrophy and hyperplasia of the thyroid gland which, in this series of cases, were about evenly distributed throughout the gland; that is, in some areas one encountered lobules made up purely of small round acini containing practically no colloid, or if any, at the most a mere drop. The small acini were closely packed together, being held by a very delicate stroma through which coursed many dilated blood vessels. The more developed of these smaller acini seemed to occur toward the center of the lobule, the younger ones being arranged in the periphery (fig. 1). The epithelial cells in these small acini were so closely arranged that their apexes abutted on each other (fig. 19). The other types of hypertrophy and hyperplasia referred to were the larger lacelike papillomatous acini which were very irregular in shape and uniformly larger in size (figs. 1, 6 and 10). In some lobules the two types of hypertrophy were present together and in this event the larger lacelike acini, as a rule,

were in a more central situation with the smaller acini toward the periphery. The colloid was very scant and in many acini totally absent; when present it stained very poorly, being shreddy, granular, vacuolated and watery-like in appearance (figs. 1, 6 and 10). The vacuoles, as a rule, were interposed between the central portion of the colloid and the edges of the epithelium. The papillomatous infolding of the epithelium, in the majority of these larger acini, almost completely filled the lumen



Fig. 13 (case 3).—Area of hyperinvolution in large colloid cyst developing during involution ($\times 40$); flattened epithelium lining cyst which contains densely stained colloid without any vacuoles; compression of tissue about cyst evident; development of capsule from intralobular and interlobular stroma is shown, also flattening of small peripheral acini.

so that the spaces available for the collection of colloid appeared as mere slits in the lobules (fig. 1). Occasionally acini were found which contained large numbers of desquamated epithelial cells and red blood cells (figs. 1, 6 and 10).

The epithelium differed slightly in the large and small acini but on the whole showed the same fundamental changes. In the larger acini the epithelial cells were tall, columnar cells and very active in appearance (fig. 2). These cells stained lightly and contained large vesicular nuclei which were situated at the base of the cells. The contour of the cell, besides being columnar, was somewhat barrel shaped, being convex at the apex and along the sides, the cells seeming to bulge with their



Fig. 14 (case 4).—Areas of hyperinvolvement that had resulted in the formation of two large colloid cysts ($\times 16$); this is a very low power photograph; these areas developed during involution. The histologic appearance and microscopic structure of the thyroid gland of patients 4 and 5 before involution were similar in all respects to those of patients 1, 2 and 3; therefore it was not felt necessary to print them.

contents or presecretion bodies. The cytoplasm contained numerous mitochondria which did not appear to have any special polarity but were diffusely scattered throughout the cell. They occurred in rods of different lengths and shape. The chromophobe vacuoles were numerous and

stood out because of the inability to stain them. They seemed to be situated in a fine, granular network of cytoplasm which took a faint pink stain. Colloid droplets were not infrequently observed; they were usually situated in the apical end of the cell or alongside the nucleus, being best seen with Bensley's mitachondrial stain or neutral gentian violet. It would seem that these colloid droplets were much more scarce in the very active gland. The nuclei contained a fine chromatin network



Fig. 15 (case 4).—Areas of extreme hyperinvolution termed in this study as the third type that approximates degeneration ($\times 67$); inequality in size of acini, extreme involution of epithelium and pyknotic nuclei; disintegrating acini, with the result that small clumps of epithelium are deposited in the abundant stroma; the stroma here is partly made up of colloid which has escaped from the acini due to this disintegration; this type of disintegration is frequently seen in areas of extreme involution.

with granules and from one to three nucleoli. Frequent mitotic figures were seen. In the smaller acini, the epithelial cells were not, as a rule, as high as the columnar cells of the larger acini but were more square in shape, being a rather low columnar cell. Otherwise, these cells did not

differ materially from the high columnar cells. Occasionally, a marked disparity was observed in the size of the nuclei of the small acini. In these sections, shown in figures 1, 2, 6 and 10, there are minor variations in the height of the epithelium, the size and the shape of the acini and the density and amount of the colloid, but as a rule the process of hypertrophy and hyperplasia is a diffuse, fairly uniform one.

MICROSCOPIC CHANGES IN THE THYROID GLAND CONCOMITANT
WITH AN ARTIFICIAL REMISSION RESULTING FROM THE
ADMINISTRATION OF IODINE: INVOLUTION OF THE
THYROID GLAND IN EXOPHTHALMIC GOITER

Gross Appearance.—The thyroid gland in the gross was much changed. The surface instead of being smooth presented nodules and elevations varying from 0.5 to 3 or more centimeters in diameter. The gland seemed to be definitely less mobile in the neck in all directions, being bound down by periglandular adhesions. The normal fascial cleavage was disturbed and to a great extent abolished. The vascularity seemed definitely decreased, both arterial and venous. The gland itself was much more difficult to mobilize at operation and seemed to be more brittle and stiff, having lost to a great extent its elasticity. The capsule seemed bulging with the contained lobulated parenchyma and definitely thickened. On section the cut surface of the gland was glary in appearance, and from it a clear lymphlike fluid dripped, suggesting that there was obstruction to the flow of lymph in the gland—a backing up of the lymph, due to an interference with the free outflow. Cystlike areas that seemed to be filled with fluid and also dilated, localized areas of colloid could be noted in the gross (fig. 20). Besides these there were areas with a smaller amount of colloid which were more opaque and somewhat granular, appearing as elevated areas of parenchyma on the cut surface and giving one the impression of small adenomatous areas.

MICROSCOPIC APPEARANCE AFTER INVOLUTION HAS OCCURRED AS
A RESULT OF IODINE ADMINISTRATION AND AN
ARTIFICIAL REMISSION

The sections showed the most striking alterations when compared to the microscopic sections of the gland before iodine was administered (figs. 3, 4, 7, 11 and 12). The connective tissue elements were markedly increased in not only the interlobular and intralobular stroma or septums but also in the scarring throughout the gland. In some instances, this approached a true sclerosis of the gland. By far the most striking and significant change observed was the increase in amount of colloid and the definite change in its character. After iodine it was more heavily and uniformly stained, homogeneous, distending the acini to their capacity

and in some instances even beyond this capacity. There were still to be found areas of vacuolization of the colloid but in a far less marked degree than before iodine was given (fig. 11). The acini were much more regular in shape and size, being ballooned out as it were by the colloid until, to a great extent, the histologic picture of the normal gland was approximated, at least as near as it is possible for a thyroid gland to approximate normal, having once been the seat of hypertrophy and hyperplasia. The small, as well as the large, acini contained the same type of colloid. Some infolding of the epithelium was present, but this was much less marked and these occasional sprigs and mounds of epithelium remained as evidence of the involution of a previous hypertrophy and



Fig. 16 (case 5).—Section across entire portion of base of right lobe which contains two large colloid cysts that were developed during involution and could be palpated clinically before operation ($\times 10$); however, before the administration of iodine or the completion of involution there were no such areas demonstrable either clinically or microscopically.

hyperplasia of the parenchyma. The lobulation of the gland was not quite as evident because of the distention of the acini and the stretching with the consequent thinning out which the septums must undergo. The same intralobular pattern of the lobule or division into acini was present, the smaller ones situated more peripherally and in some instances completely compressed or flattened. The blood vessels and lymphatics were much less apparent, being partially occluded and collapsed in the interlobular and intralobular septums by the pressure resulting from the marked increase in colloid. The epithelium lining the acini showed most extraordinary alterations when compared with the epithelium lining the acini in the glands before iodine was given. Figures 1 and 3, 2 and 4, 6 and 7, and

10 and 11 should be compared. After iodine and involution the epithelial cells were much decreased in size in general throughout the section, but in some places the decrease was greater than in others. There was always a marked diminution from the columnar type to a cuboidal or low columnar cell and in the areas of complete involution the epithelial cells not only were of the size of the normal thyroid cell but also approximated that of an endothelial cell, being flattened so much that the nuclei pro-

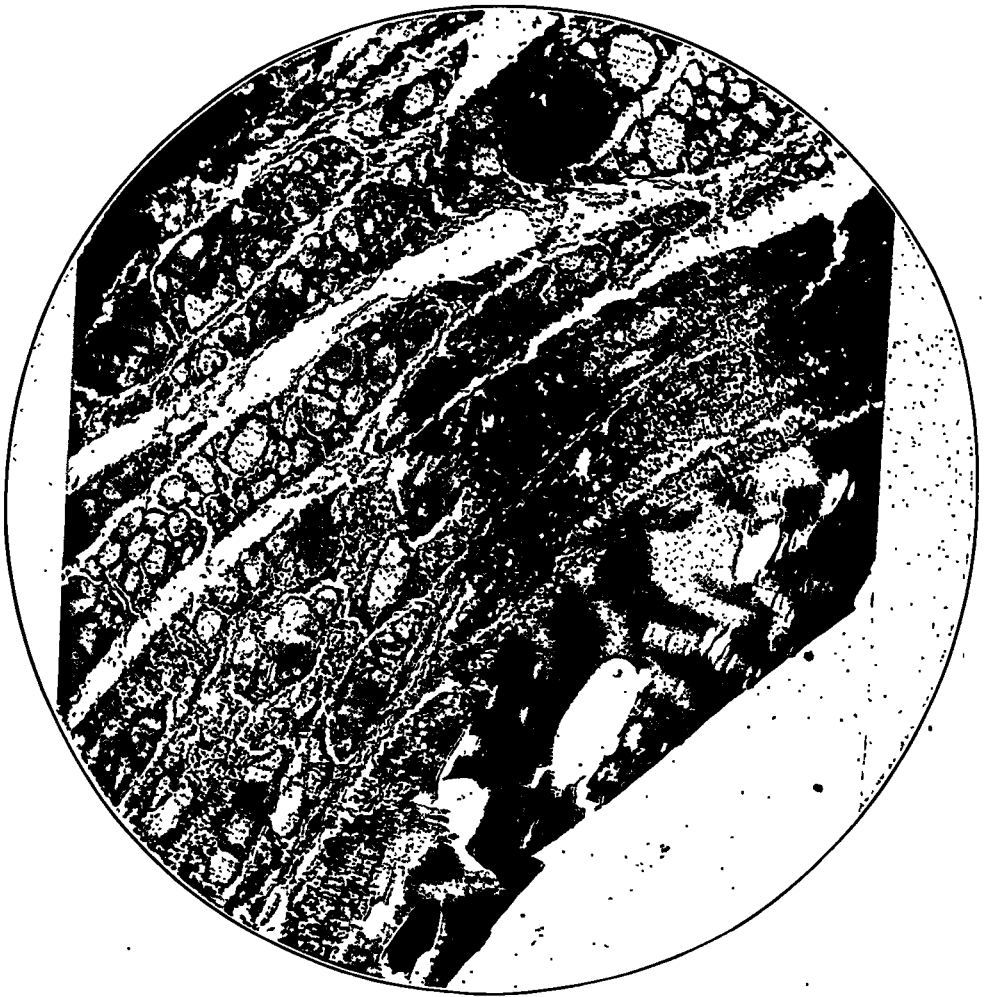


Fig. 17 (case 5).—Section taken through margin of colloid cyst shown in figure 16 ($\times 16$); average amount of involution of gland as a whole can be seen in tissue adjacent to the colloid cyst; compression of parenchyma and flattening of peripherally placed acini due to pressure of cyst against the intralobular and interlobular stroma, which is progressing to the formation of a capsule; cyst lined with flattened epithelium.

truded beyond the cytoplasm like the pearls in a pearl necklace. The cytoplasm was much diminished in amount and the nucleus made up the main portion of the cell, so that one may say that as far as the epithelium was concerned the thyroid gland, during involution generally or diffusely,

undergoes more complete involution at certain points than at others. The tendency in general was toward complete involution and the epithelium approximated very closely the type of epithelium one sees in the simple colloid goiter. The shape of the cells also differed from that of the gland of an uninvoluted exophthalmic goiter, in that they were shrunk in appearance, the lateral walls and apexes being concave instead of convex. They seemed to have rid themselves of their intracellular contents and gave the appearance of a resting or inactive cell. The ends of the cells abutted on the colloid in the majority of acini; occasionally, however, a small number of clear vacuoles were interposed between the colloid and the apexes of the epithelial cells. The cytoplasm stained a more even pink and had lost entirely the mottled appearance seen in the exophthalmic goiters before iodine was given. No chromophobe vacuoles were observed and the cytoplasm seemed to contain many finely divided granules which were distributed evenly and diffusely throughout the cell. The mitochondria were much reduced in number and instead of appearing as rodlike structures were broken up into small granules which were also distributed diffusely throughout the cytoplasm with no especial polarity. Little difference could be ascertained in the number and size of the colloid droplets. With Bensley's method of staining for mitochondria these colloid droplets took on a rather green stain, and seemed to be situated in the apical end of the cell, near the nucleus, as a rule. The nuclei were very pyknotic and shrunk. The nucleoli were difficult to see and the chromatin granules seemed to be more numerous, causing the nuclei to be much more densely stained or basophilic. No mitotic figures were seen. The areas of lymphocytosis were much less frequent during and after involution and the areas that were present seemed to be markedly reduced in size. The general appearance of a section of the thyroid gland after iodine had been given, and a complete involution brought about, seemed to be that of a resting or inactive state of the epithelium which appeared in marked contrast to the previous condition of extreme cellular activity in the same gland before the involutional changes had occurred.

The foregoing description applies to the involutionary changes that occurred in each of the seven cases of this series of exophthalmic goiter during an artificial remission that occupied a period of time from ten to thirty days, and represents the average degree of involution that was observed to occur throughout the gland as a whole. For the sake of clearness, the degree of involution above described will be referred to as the normal and average amount occurring in the cases of this series, and the variations now to be described will be classified according to their relation to this average normal whether greater than normal or hyperinvolved, or less than normal or hypo-involved.

HYPERINVOLUTION

The areas of hyperinvolution observed to develop in this series of seven controlled cases could be divided roughly into three distinct types. The first type was the large colloid cyst (figs. 5, 13, 14, 16 and 20). These varied in size and number and could be found diffusely scattered throughout the gland. They usually occupied one lobule and were lined with a single layer of cuboidal epithelium, which closely approximated a normal thyroid cell in size, shape and staining capacity. There were

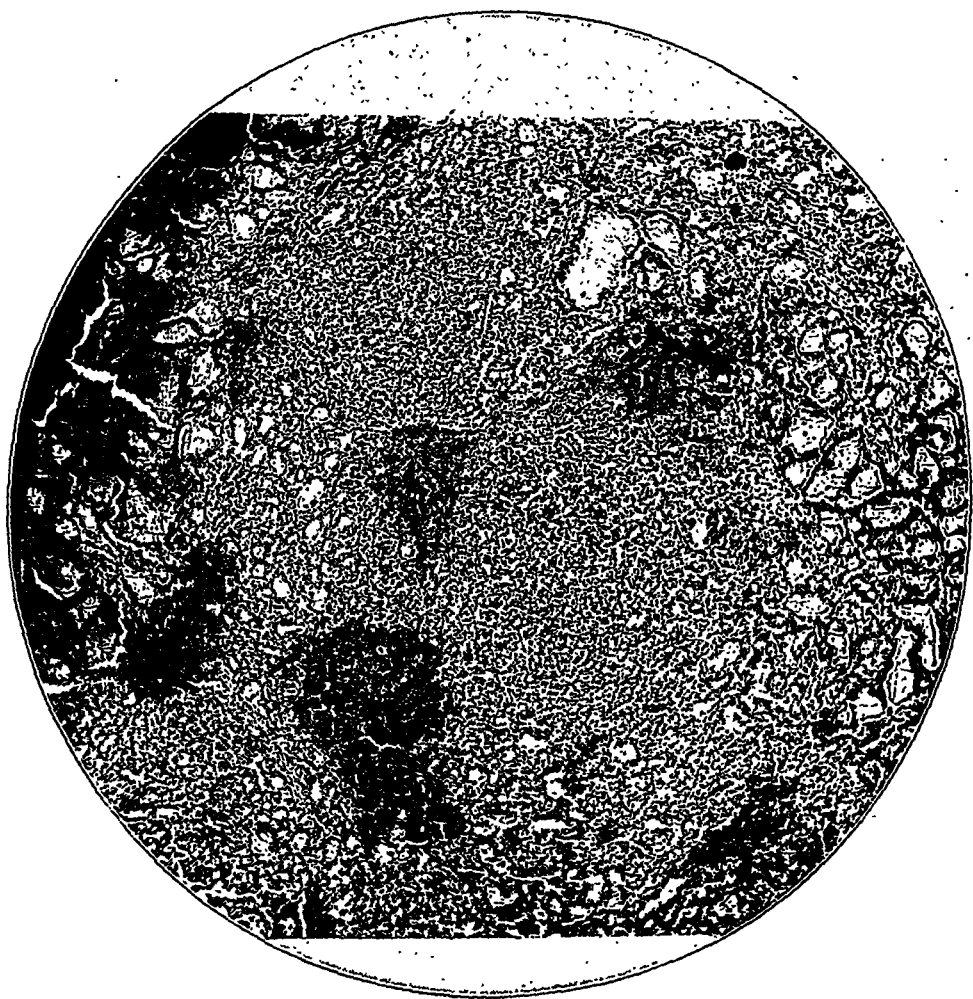


Fig. 18 (case 5).—Section from left lobe of the gland of patient 5 after three weeks' treatment of iodine and a complete clinical remission, showing areas of persistent hyperplasia of three distinct lobules (40 mm. lens); it is noted that the lymphocytes in these areas are pronounced; the adjoining gland can be seen at the periphery to have undergone the normal or average amount of involution occurring throughout the gland, these areas of hyperplasia persisting; from the area in the marked circle figure 19 is made; these areas have been described by various authors as miliary and diffuse adenomas; they are merely areas of persistent hyperplasia.

areas in which the lining epithelium was absent but these areas were probably artefacts. The epithelium was occasionally more flattened and approximated the endothelial type of cell. These cysts contained a large amount of homogeneous, even staining colloid which abutted on the apexes of the epithelial cells. About the periphery of these cysts, there was compressed normal involuted thyroid gland tissue which in general was made up of flattened small acini, intralobular and interlobular sep-

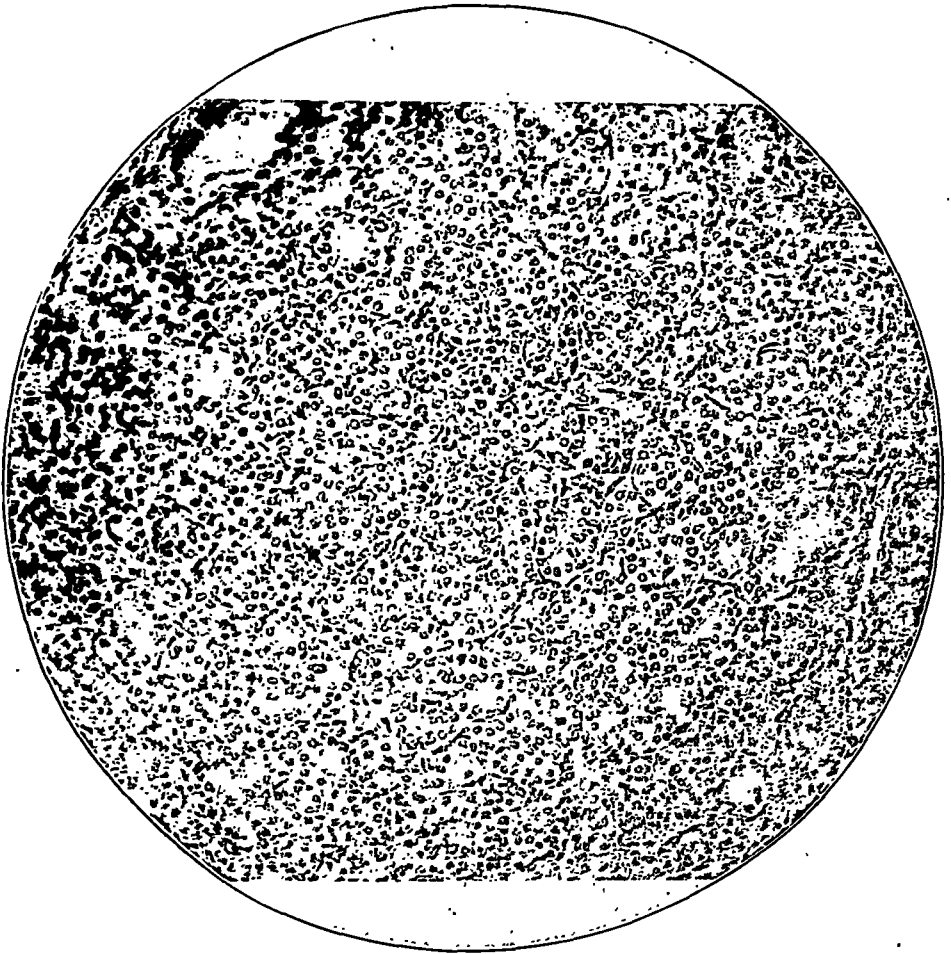


Fig. 19 (case 5).—Area described in figure 18 by circle under higher magnification ($\times 176$ mm.); persistent area of hyperplasia with closely packed small acini of the type seen in fetal and infant thyroids is shown; cells lining acini do not show involutionary changes and colloid is striking by its absence.

tums (figs 13 and 17). In these the early stages of actual atrophy and substitution of this parenchyma by connective tissue between the cyst wall and the intralobular septums had not occurred, but it is believed that it would occur if the element of time had been longer, resulting in the formation of a definite connective tissue capsule. The second type of hyperinvolution manifested was in localized areas of very much

dilated acini, filled with colloid and well circumscribed or encapsulated with compressed parenchyma, as well as the interlobular and intralobular septums; these areas were histologically indistinguishable from the so-called colloid adenomas (figs. 5, 8 and 9). These areas were confined to one lobule and were diffusely deposited throughout the entire gland, no sections being entirely free of them, whereas large portions of the same gland, including many sections, removed before iodine was given or before an involution was brought about, showed no areas of this type. These dilated acini were so much larger than the acini of the average glandular tissue about the lobule that they could be seen in the gross (fig. 20) and appeared in all respects similar to the so-called colloid adenomas. The large acini themselves varied quite markedly in size and shape, being larger than the normal acinus but still varying in size with respect to each other. The epithelium was always flattened

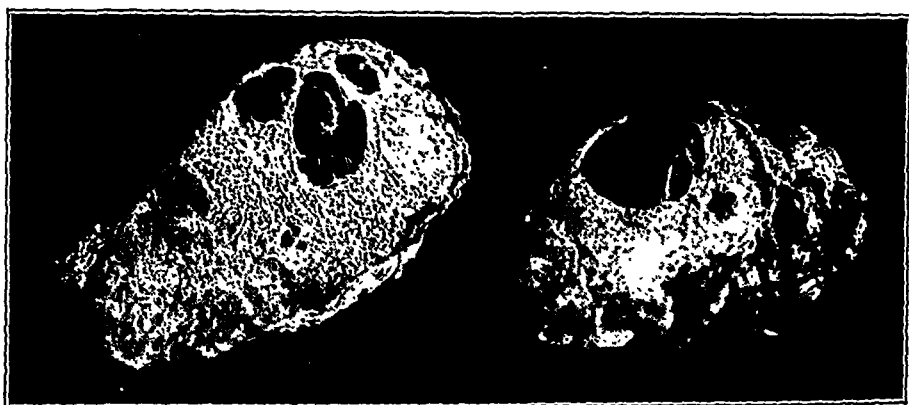


Fig. 20.—Gross involutinal changes observed to occur following the administration of iodine and during a marked clinical remission of a case of exophthalmic goiter ($\times 10$).

out like an endothelial cell with the nucleus as the most prominent part of the cell. The cytoplasm was scant and the cytoplasmic bodies were difficult to see. In none of these hyperinvolved areas were there any vacuoles to be seen in the colloid. The involution here caused a regression slightly beyond normal as defined above, being manifested by the size of the acini, the amount of colloid and the extreme flattening and regression of the epithelial cells. It was a very characteristic feature that the interacinous stroma in these areas was quite delicate and thin, and confluence of these acini was not infrequently seen, probably due to the rupture of this delicate stroma at some point, this rupture resulting, no doubt, from nutritive disturbances secondary to the marked distention. The involution of the parenchyma immediately surrounding these areas of hyperinvolution was usually typical of the degree of involution occurring in the gland as a whole (fig. 9). The third type of hyperinvolution observed to develop in this series of cases was one that

far exceeded the normal amount of involution, going on to a state approximating a degeneration of the thyroid parenchyma and usually associated with both of the foregoing types, namely, the cysts and also the areas of hyperinvolution or encapsulated large dilated colloid acini resembling the so-called colloid adenomas. In these areas of extreme involution, one was impressed with the abundance of the material forming the stroma and the paucity of the sparsely situated acini (fig. 15). The acini and their remnants seemed to be literally buried in the large amount of stroma. The latter was composed largely of colloid similar in all respects to that occurring in the acini and was homogeneous and even staining throughout. The stroma was delicate though abundant and seemed to be everywhere filled with this extra-acinous colloid which apparently had escaped into the interacinous areas as a result of the disintegration of the acini. The acini varied in size from that approximating the normal acinus of the thyroid gland down through the smaller grades to small clumps of epithelium consisting of two, three and four cells, grouped in clusters and between which no lumen could be made out. Occasionally, one saw single epithelial cells, while the epithelium as a whole, especially the number of acini, was markedly decreased per lobule in these areas, below the amount present in the normal thyroid gland. The epithelial cells in these areas were low, flat and shrunken, the epithelium was very inactive and seemed to be degenerating in most instances; it was very granular and contained many colloid droplets. The nuclei were markedly shrunken and pyknotic and could often be seen extracellular in the stroma. It is interesting to note that the same type of extreme involutional change is to be found also in the so-called fetal and mixed fetal and colloid adenomas.

AREAS OF HYPO-INVOLUTION

In the other type of involutional bodies which were mentioned, the hypo-involutated areas, it was stated that there were islands or lobules in the glands of exophthalmic goiter which seemed to resist involutional changes or the factors that were efficacious in bringing about the involution of the remainder of the gland. These areas were confined to one lobule, but several such areas were often encountered in one section and, as a rule, seemed to be diffusely scattered throughout the gland. About these areas a localized infiltration of the stroma with small lymphocytes (fig. 18) much more marked than in the remaining portions of the gland, occurred. These areas of hypo-involution were made up of small round acini closely crowded together and containing very small lumina, if any at all (figs. 18 and 19), with the apexes of the cells abutting on each other. There seemed to be such a rapid growth of small acini in the center of the lobule that a great deal of pressure was produced on the peripherally situated parenchyma, against the interlobular



Figure 21



Figure 22

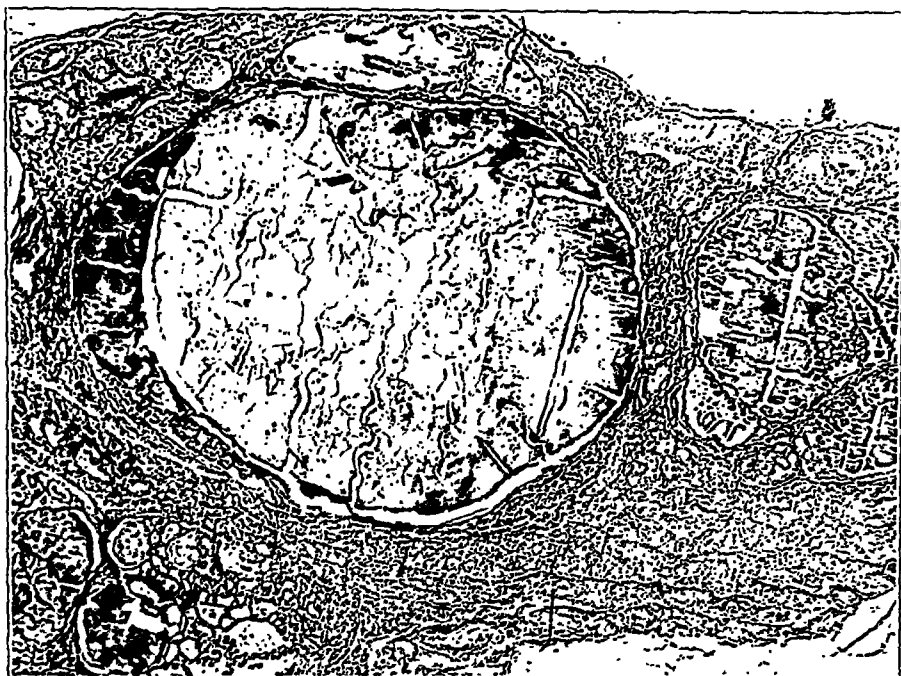


Figure 23

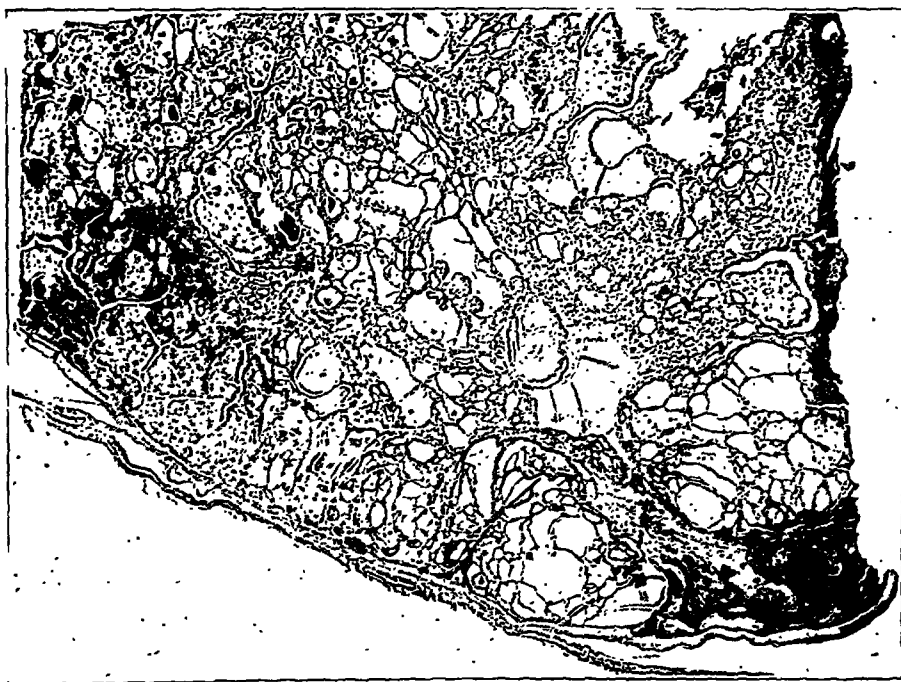


Figure 24

Figs. 21, 22, 23 and 24.—Areas of hyperinvolution that have occurred in the four cases mentioned in the text in the thyroid gland of patients undergoing spontaneous remissions and in which a subsequent exacerbation had occurred when they were removed by operation ($\times 16$); the histologic alterations observed in these cases following a spontaneous involution will be seen to correspond exactly with the involutional changes following an artificial remission or involution.

septums. It did not seem at all clear why these specific areas persisted as centers of active growth while the remainder of the gland underwent involutionary changes throughout, even in the lobules adjacent to those resisting involution (fig. 18). The epithelial cells of the hypo-involved areas approximated closely the epithelial cell of an active hyperplasia and did not show the involutional changes that were observed in the epithelium in the gland about these areas.

In figure 18 this type of parenchymatous hypertrophy may be seen and represents a well defined encapsulated area of persistent hyperplasia. All that can be said, however, in regard to these areas is that they are localized encapsulated areas of hyperplasia which seemed to resist the involutional changes brought about in the remainder of the gland by the use of iodine. They do not seem to obey the laws governing the remainder of the gland in regard to involution.

SPONTANEOUS INVOLUTION

To demonstrate further the point of involution of the thyroid gland in exophthalmic goiter in figures 21 to 24 are shown microscopic sections from four cases of typical exophthalmic goiters of more than twelve years' standing before operation, and in which unquestionable remissions and exacerbations occurred over six times, including the last exacerbation in each case. After each remission there was noted the appearance of lumps or nodules in the thyroid gland; these nodules increased in size over a period of years. The same involutional changes were observed in these cases that have been noted to have occurred in the seven controlled cases. The lobules containing the large dilated colloid acini and cysts or areas of hyperinvolution were the involutional changes that were established following a previous hypertrophy and hyperplasia and in these instances a secondary hypertrophy had been engrafted on these hyperinvolved areas or lobules concomitant with the last exacerbation. No doubt another involution would enlarge them still more and they would again become Basedowified in another exacerbation.

Clinically, these patients had typical cases of exophthalmic goiter with the exception of the thyroid gland, which was nodular and felt as though it might be the seat of adenomas, in the true sense of the word. The changes observed in the foregoing study of the controlled cases that have been cited render the interpretation of these apparent clinical and pathologic disparities possible. We have at the same time a typical picture, clinically and histologically, of exophthalmic goiter associated with areas resembling the so-called colloid adenomas but which in truth were not adenomas at all, but merely areas of hyperinvolution following a previous hypertrophy and hyperplasia of the thyroid gland, which had again become involved in the current exacerbation and had again undergone hypertrophy and hyperplasia in sympathy with the remainder of

the gland. To prove further the similarity of the involutional changes observed to occur in the seven cases that were controlled and those occurring spontaneously as well as artificially following an iodine remission, fifty patients with exophthalmic goiter who had received iodine were studied and in all these areas of hyperinvolution occurred accompanying a clinical remission. In five other cases which were refractive to iodine these involutional changes were not observed. From 1900 to 1910, in fifty cases of exophthalmic goiter that had an acute onset and a fulminating course without remission, no involutional changes could be demonstrated in the entire gland, while in fifty cases of exophthalmic goiter in which iodine was not administered but in which there was a history of one or more remissions, these involutional changes were found in great abundance.

COMMENT

In this series of seven cases of exophthalmic goiter the histologic structure of the thyroid gland was studied before and after a clinical remission was established. The clinical improvement and fall in the basal metabolic rate during a remission was accompanied by a transformation in the microscopic appearance of the thyroid gland from that of an extreme hypertrophy and hyperplasia of the parenchyma to that of a resting or colloid state. The resting state of involution was characterized by: (1) increase in the amount of colloid; (2) increase in the connective tissue in the gland; (3) decrease in the vascularity; (4) increase in the size and regularity of the acini; (5) decrease in the height of the epithelium; (6) decrease in the cytoplasmic bodies in the epithelial cells, and (7) decrease in mitosis and lymphocytic infiltration. The latter state was thus shown to be less active, physiologically as well as histologically, than the former state of hypertrophy and hyperplasia. This transformation was called an involution or regression of the hyperplastic thyroid gland in an attempt to reapproximate the histologic structure of the normal thyroid gland. The process of involution is, as a rule, a diffuse one occurring throughout the gland as a whole to about the same degree, except that in certain areas the involution is more or less complete. The average degree of involution observed to occur in this series of seven controlled cases and fifty other cases in which iodine was given has been termed the normal degree of involution occurring during a remission. Involutional changes, more pronounced or in a greater degree as well as in a less degree than normal, were encountered and referred to as areas of hyperinvolution and hypo-involution. The areas of hyperinvolution or involutional bodies were divided into three types: first, the formation of colloid cysts; second, localized and encapsulated areas of dilated colloid acini, histologically indistinguishable from so-called adenomas, and, third, areas or lobules in which

the involution and regression had gone beyond the average or normal amount of involution for that gland to a state of degeneration, characterized by a disparity in the size and paucity of sparsely situated acini in an abundant stroma, which was made up of an increased amount of fibrous tissue and an extra-acinous colloid. Histologically, the areas appeared very similar to the mixed adenomas or fetal and colloid adenomas. No evidence of the formation of new tissue could be made out in these areas and in the latter respect they are again similar to the adenomatous areas named. In the tissue removed before iodine was given no such areas could be found. However, after involution of the gland had occurred these areas of hyperinvolution were abundant. The appearance of these specific areas simultaneous with a remission would seem to indicate that they had their origin in the histologic transformation accompanying involution of the thyroid gland. For this reason they have been termed areas of hyperinvolution. These areas of hyperinvolution were found in this study to be confined usually to one lobule of the thyroid gland, the entire lobule being affected throughout and not only in one portion of a lobule; this fact suggests strongly that the changes observed may have been due to a disturbance either in the lymphatic drainage or in the circulation of the lobule or both. The epithelial elements of these areas showed the most extreme involutional changes and appearance of inactivity. It was pointed out that the localized distention of the acini by the colloid caused a peripheral pressure on the fibrous tissue envelop surrounding the lobule. Evidence of this pressure could be seen by the flattening of the peripherally situated acini against the interlobular septums. Because the arteries in the lobule are, in the main, end arteries and also because of the rapidity with which the involutional changes occur (from ten to fourteen days) there is not time for the adaptation of the circulatory bed of the acinus to this marked stretching and distention. Thus, degenerative changes resulting from circulatory embarrassment due to this stretching and probably occlusion of the smaller branches, at least, are very common, a relative pressure anemia resulting. There were certain lobules, mentioned above, of the thyroid gland in these seven cases of exophthalmic goiter which resisted the factors that were efficacious in bringing about the involutional changes in the remainder of the gland and these lobules have been termed areas of hypo-involution. It was pointed out that the parenchyma surrounding these areas of hyperinvolution and also hypo-involution was always fairly representative of the normal amount of involution occurring throughout the gland as a whole. These areas of persistent hyperplasia were always confined to one lobule and seemed to be, at the same time, areas in which lymphocytic infiltration also persisted and was most marked. They appeared to be histologically similar

to the areas described by Ewing as "miliary adenomata." It was not thought in this study, that any more could be said than that they were areas of persistent hypertrophy and hyperplasia which did not obey the laws governing the involution of the gland as a whole. In the true sense of the word, these areas were not adenomatous for the reason that the structure of the gland was maintained throughout; the general stimulus of hypertrophy and hyperplasia in the gland, as a whole, has been followed in these localized areas or lobules, and there is no evidence of new tissue formation. However, these areas were interesting because they may well serve to explain the temporary beneficial effect or remission following the use of iodine and also why the patient, clinically, cannot be brought to the status of a normal individual by the use of iodine, always being in a state of low grade hyperthyroidism. It is also not felt that the areas of hyperinvolution or persistent colloid bodies are in any sense adenomatous and for the same reasons which are mentioned above, namely, because they maintain the normal histologic structure of the gland; there is no evidence of new tissue formation, and the general stimulus to hypertrophy and hyperplasia of the gland, as a whole, is obeyed in these areas. Cases are shown in this study which have undergone a spontaneous remission and in the glands of which the same type of involutional bodies have been found. Also, in the latter cases, there has been in a subsequent exacerbation, a reinvolvement of these hyperinvolved areas in the hypertrophy and hyperplasia that has occurred throughout the gland as a whole. It would seem only natural that, given an acinus of normal dimensions which undergoes marked hypertrophy and hyperplasia of the epithelial lining causing it to be folded in on itself with the formation of smaller peripheral acini, would, when ballooned out or distended with a marked deposition of colloid, be much increased in size. When the epithelial lining became infolded, the size of the follicle conformed to the size of the connective tissue capsule surrounding it. But the increased pressure due to the increased amount of colloid causes the filling up of the vesicle to the size of its inner or epithelial lining, thus increasing the size of the acinus, the lobule and ultimately the lobe and entire gland. Subsequent hypertrophies and hyperplasia of the lining epithelium result in another infolding which again becomes ballooned out to a still larger dimension with each involution and so on, *ad infinitum*, so that a lobule, lobe or even a thyroid gland which is once the site of hyperinvolution actually grows in size with each subsequent hypertrophy and involution. It is very interesting to note that the migrating type or substernal type of exophthalmic goiter is confined entirely to this type of gland which shows signs of previous involutional changes. The consequent growth and actual increase in tissue as a result of these changes forces the gland

into the mediastinum. The acute fulminating cases of exophthalmic goiter as a rule are not substernal.

Fifty cases of exophthalmic goiter in which iodine treatments were given and in which a clinical remission was established were cited and in all of these areas of hyperinvolution occurred. In fifty cases of exophthalmic goiter, from 1900 to 1910, in which the clinical course had been acute and unremitting, no involutional changes or bodies were observed. In five cases that were refractive to iodine, no involutional changes could be demonstrated. In all the cases of exophthalmic goiter in which the history of one or more spontaneous remissions and exacerbations could be obtained these involutional bodies or areas of hyperinvolution were found in abundance. They differed in size throughout the same gland but in the cases that underwent a spontaneous remission they were definitely palpable, clinically, and were noted to enlarge with each exacerbation and remission. There seems to have been a steady enlargement over a period of years in the latter cases, in which steady enlargement was at times accelerated.

If one digresses for the moment from the pathologic hypertrophies and considers the physiologic hypertrophies, interesting problems immediately arise, which of course will have to be investigated in great detail. Involution of the thyroid gland in this series of cases occurred following pathologic hypertrophy and hyperplasia; nevertheless, the histologic changes of involution would in all probability be the same regardless of the cause of the hypertrophy, whether it be physiologic or pathologic, and the microscopic structure and appearance of the thyroid gland as a result of an involution would be constant. So far as it is known, nodular goiter has not occurred in childhood before the onset of the prepuberty and puberty hypertrophy, that is, before 8 or 10 years of age. Following these physiologic hypertrophies involutional changes occur in the same manner as involution occurring after a pathologic hypertrophy. In the female, of course, there is to be added to this the pregnancy plus lactation hypertrophies. The greatest incidence of nodular goiter is between the ages of 12 and 40, or during the period of life in which physiologic hypertrophies most frequently occur. The milder degrees of hypertrophy and hyperplasia are in turn associated with less striking involutional changes, but the same type of involution does occur. In a yet incomplete study, in this clinic, of the available material following physiologic hypertrophies, these areas of hyperinvolution have been by far the greatest factor in producing palpable nodules in the thyroid gland. At present it seems highly probable that the majority of these nodules present in otherwise normal thyroid glands may have had their origin in the involution of a physiologic hypertrophy and are not benign neoplasms or true adenomas but areas of hyperinvolution or involutional bodies. At the present time it cannot be stated

definitely until a careful investigation of the different types of nodular goiter that occur during this period has been made and histologically reclassified. This is being done at the present time, and will be reported later. From the evidence at present, it would seem that most of these tumors palpable in nodular goiters are nothing more than involutional bodies of the same type as have been described above, and that a great many, in fact nearly all of the cases of nodular goiter with or without hyperthyroidism which have been described as colloid adenomas, mixed fetal and colloid adenomas, colloid cysts, cystic adenomas and miliary adenomas are in no sense of the word adenomatous but the result of an attempt on the part of the thyroid gland, following an hypertrophy, to reapproximate its normal histologic structure, namely, involutional bodies or areas of hyperinvolution and hypo-involution. It is not to be gathered from this article that all nodular goiters are involutional bodies because this is undoubtedly not the case; there are, without question, true parenchymatous adenomas that have been improperly described as fetal adenomas and there also are localized areas of persistent hypertrophy and hyperplasia which have been described as miliary and diffuse adenomas. Whether or not these should be called adenomas is not certain. There are, too, the malignant tumors. Histologically, however, the involutional changes in the thyroid gland are quite as definite as the hypertrophic and hyperplastic changes and should be considered so. The occurrence of the above noted involutional bodies must in the future be taken into consideration and separated in the pathologic classification from true adenomas. For a proper comprehension and interpretation of the pathologic processes which are encountered in a study of the diseases of the thyroid gland, the changes in the microscopic structure during involution and the deposition of these involutional bodies must be taken into consideration.

CONCLUSIONS

1. Associated with a clinical remission, whether artificial or spontaneous, in cases of exophthalmic goiter, involutional changes in the histologic structure of the thyroid gland occur which are just as definite and fundamental as the microscopic alterations occurring during hypertrophy and hyperplasia.

2. These involutional changes may be divided into three different types: (1) normal or average degree of microscopic alteration occurring throughout the gland as a whole; (2) areas of hyperinvolution, and (3) areas of hypo-involution.

3. The normal or average extent of involution occurring in a case of exophthalmic goiter during a clinical remission represents the nearest

return to the normal histologic structure of the thyroid gland that can take place in a gland once the site of an hypertrophy and hyperplasia.

4. The normal or average degree of involution occurring during a remission in this series of seven cases was characterized by: (a) increased amount and density of colloid; (b) increase in size and regularity of acini; (c) increase in amount of connective tissue in the septums and scarring throughout the gland; (d) decrease in size and height and change in shape of epithelial cells from a high columnar to a cuboidal or endothelial cell; (e) decrease in cytoplasmic bodies or constituents; (f) decrease in vascularity of gland, and (g) decrease in vacuolization of colloid and deposits of lymphocytes.

5. Areas of hyperinvolution correspond, clinically and histologically, to the so-called colloid adenomas, cystic adenomas, fetal and colloid or mixed adenomas and colloid cysts.

6. The areas of hypo-involution are localized encapsulated areas of persistent hypertrophy and hyperplasia and have been termed miliary adenomas by Ewing and diffuse adenomas by others.

7. Involution of the thyroid gland occurs following hypertrophy and hyperplasia whether this be physiologic or pathologic.

8. These areas of hyperinvolution and hypo-involution are not benign neoplasms of the thyroid gland or adenomas in the true sense but merely residual histologic alterations occurring during an involution of the thyroid gland following an hypertrophy and hyperplasia.

9. These areas of hyperinvolution or involutional bodies may undergo subsequent microscopic alterations denoting hypertrophy and hyperplasia in sympathy with the changes occurring in the gland as a whole. Thus, an increase in their size may occur following each exacerbation and remission.

10. In this study of the seven controlled cases these involutional bodies were directly observed to occur. In fifty cases of exophthalmic goiter undergoing spontaneous remissions and subsequent exacerbations, the same involutional structures were observed in all degrees of development. In fifty cases in which iodine treatment was given areas of hyperinvolution occurred in abundance.

11. The presence of new tissue formation was not found in any of the areas of hyperinvolution.

12. True parenchymatous or fetal adenomas of the thyroid gland do occur but should not be confused with the involutional bodies that are not adenomas.

13. In order properly to interpret the many and bizarre microscopic alterations observed in a study of the diseases of the thyroid gland, a knowledge of the histologic changes occurring during involution is necessary.

THE TRANSPLANTATION OF BONE INTO JOINTS*

S. L. HAAS, M.D.

SAN FRANCISCO

Various attempts to obtain tissue culture of bone have been reported, but thus far there has been no convincing proof or satisfactory demonstration of the growth of bone outside the body. These failures are not surprising when one thinks of the structure of bone with its normal intricate method of growth and repair in response to some physiologic stimulus.

In seeking for a substitute for an artificial culture medium, it was thought that a joint cavity would serve the purpose and act as natural incubator for bone tissue. A joint cavity was selected because it was thought that the synovial fluid would serve as a source of nourishment for young growing cartilage and osteoid tissue. It was also expected that the implanted segments of bone would produce a synovitis and that the excess of fluid, as well as the motion of the joint, would tend to keep the pieces of bone moving and prevent them from becoming adherent to the synovial membrane.

It may be well to recall some of the findings of the investigations on the behavior of loose bodies in joints, so far as they have a bearing on the present experiments. Strangeway¹ believes that articular cartilage derives its nutriment from synovial fluid and that loose cartilaginous bodies not only survive in the joint cavities but also may increase in size.

Fisher² does not agree entirely with Strangeway that the synovial fluid is the normal source of nourishment for articular cartilage. He asserts that there are two other possibilities; namely, (a) plasma extruded from capillaries lying in the cancellous plates abutting on the calcified layer, (b) plasma extruded from the plexes of vessels lying beneath the synovia at the margin of the articular cartilage. Fisher believes that cartilage cells, free in a joint, retain their vitality in almost every case and after a time actively proliferate. He states that the majority of bone corpuscles die, as do the contents of the bony spaces. There is never any sign of proliferation of the osteoblasts with the

* From the Surgical Laboratory of Stanford University School of Medicine.

1. Strangeway, S. P.: Observation on the Nutrition of Articular Cartilage, *Brit. M. J.* 1:661 (May) 1920.

2. Fisher, A. G. T.: A Study of Loose Bodies Composed of Cartilage or of Cartilage and Bone, Occurring in Joints, with Special References to Their Pathology and Etiology, *Brit. J. Surg.* 8:493 (April) 1921.

formation of new bone. However, in case there are early adhesions to the synovial membrane there may be a proliferation of osteoblasts and the formation of new bone.

Since the present investigation was started, Ito³ has reported an interesting result of one of his experiments, in which he placed a segment of bone and cartilage in a joint cavity. He found the specimen free in the joint of a rabbit four weeks after operation. The microscopic examination showed it to be covered by a thin layer of fibrous tissue. The original cartilage had maintained itself, but in certain places the cartilage cells stained feebly and were of lowered vitality. In other places there was some well maintained cartilage proliferation. The old bone tissue had nearly lost its bone cells but slight new bone formation could be seen. The bone marrow consisted mostly of fatty cells and red bone corpuscles.

The negative finding of Fisher, on one hand, and the positive findings of Ito, on the other, leaves the solution of the problem of the growth in free segments of bone in joint cavities still unsettled. In the following investigation, several different principles were utilized which it was thought would help in the successful determination of the question; instead of using a single piece of bone, several fragments were put together, because there is a definite physiologic stimulus for union of several fragments of a transplant, just as there is in the healing of a fracture under normal conditions. Before insertion into the joint, the pieces of bone were placed in a piece of thin perforated rubber tubing to prevent adhesion to the synovial membrane and allow sufficient nutritive material to pass in through the perforations. Young animals were selected because of the greater proliferative power of young osteoid tissue and the piece of bone was obtained from a metacarpal bone or from the upper end of the fibula of the same animal. The following results were obtained in fifteen experiments on dogs and rabbits, all performed under ether anesthesia with aseptic technic.

PROTOCOLS

EXPERIMENT 1 (Dog 62, eight days).—*Operation*.—An incision was made on the outer side of the knee joint of the left leg, and extended inward along the side of the patella to the joint cavity. A second incision was made over the head of the fibula. A section of bone with its periosteum 3 cm. long was removed and broken into a number of fragments. These were placed in two separate pieces of thin rubber tubing tied at both ends and perforated on the sides. Two specimens were then dropped into the joint cavity, after which the wounds were closed in layers.

3. Ito, L. R.: The Nutrition of Articular Cartilage and Its Method of Repair, 12:31 (July) 1924.

Gross Findings.—The two pieces of tubing were found adherent to the synovial membrane. There were synéchia of organized fibrin or ingrowths from the synovial membrane extending into the perforations in the tubing. The bone itself was covered by the same new membrane.

Microscopic Findings.—The bone was surrounded by fibrin. The nuclei throughout the bone stained poorly and there was no sign of proliferation.

EXPERIMENT 2 (Dog 69, nineteen days).—*Operation.*—An incision was made on the outer side of the right knee joint, extending down over the head of the fibula. After the knee joint was opened, a section of bone with periosteum 2 cm. long was removed from the upper end of the fibula. The piece of bone was broken into several fragments which were then placed in a piece of thin rubber tubing tied at both ends and perforated on the sides. The wound was then closed in layers.

Gross Findings.—The tube was found adherent to the tissue just above the patella but was not surrounded by fibrous tissue. The bone appeared dead.

Microscopic Findings.—The greater part of the bone was surrounded by unorganized fibrin. At one end there was some granulation tissue. The nuclei of the bone took a poor stain. There were no signs of proliferation or regeneration at any place. The haversian canals in some places contained red blood corpuscles.

EXPERIMENT 3 (Dog 66, thirty-three days).—*Operation.*—The same procedure was carried out in this experiment as in Experiment 2, with the exception that one portion of fragmented bone was placed in the joint cavity without any covering of rubber tissue.

Gross Findings.—Both specimens were found attached to the synovial membrane in the quadriceps pouch. The specimens appeared viable; the one in the tubing was redder than the other. It looked as though a union of the fragments had taken place in both segments of bone.

Microscopic Findings.—In the pieces of bone that were in the tube many of the nuclei failed to stain. On the periphery there was some new bone, and in one place there was a bridge extending from one segment of bone to another. The bone about the haversian canals stained quite well and within the canals there were new blood vessels. The bone was surrounded by organizing granulation tissue and fibrin. The pieces of bone that were free and not incorporated in rubber tubing stained somewhat better than the other. At one end there was a large mass of cartilaginous callus and osteoid tissue (Fig. 1). The narrow spaces contained fibrous marrow with a considerable number of marrow elements and blood vessels.

EXPERIMENT 4 (Dog 62, thirty-six days).—*Operation.*—A piece of bone 1 cm. long was removed from the upper end of the right fibula and split longitudinally. The two segments were tied together with silk and dropped into the knee joint on the same side.

Gross Findings.—The specimen was found adherent to the synovial membrane at the upper end of the patella. The bone had undergone considerable absorption.

Microscopic Findings.—The piece of bone was encapsulated by fibrous tissue. The greater number of nuclei stained quite well; some, however, took a weak stain. There was no evidence of proliferation; on the contrary, there were signs of absorption on the surface.

EXPERIMENT 5 (Rabbit A (1), thirty-seven days).—*Operation*.—After the joint cavity was exposed, a segment of bone 1 cm. long was removed from a metatarsal bone on the same extremity. This segment of bone was fragmented and after being tied up in rubber tubing was dropped into the joint cavity.

Gross Findings.—The specimen was found attached to the synovial membrane. There was a new tissue extending through the perforation in the tube.



Fig. 1 (Experiment 3, thirty-three days).—Fragments of bone that were dropped into joint and became attached to the synovial membrane; A, new osteoid tissue; C, new cartilage.

Microscopic Findings.—The original bone took a rather poor stain. Some of the nuclei stained better than others. The marrow space contained some fairly normal looking marrow cells. There was some cancellous bone surrounding the cortical bone that had the structure of new bone but did not take a normal stain.

EXPERIMENT 6 (Dog 65, thirty-seven days).—*Operation*.—The joint cavity was exposed and one set of fragments obtained from the fibula were placed in rubber tubing and another set without tubing were dropped into the joint.

Gross Findings.—Both specimens were found adherent to the synovial membrane in the region of the subpatella fat pad. All the fragments appeared viable and united to one another.

Microscopic Findings.—The two specimens were mixed in the preparation for staining. One of the sections showed actively proliferating bone throughout with a cartilaginous knob at one end. The other showed much less new bone, it being confined to the periphery of the bone. The bone spaces in each contained a thin reticulum, rich in blood vessels.

EXPERIMENT 7 (Dog 63, forty days).—*Operation*.—A section was removed from a metatarsal bone, broken into six pieces and after being placed in rubber tubing was inserted into the left knee joint.

Gross Findings.—The tubing was attached in the region of the subpatella fat pad, and a pannus of tissue extended through the perforations. All the fragments except one appeared to be viable.

Microscopic Findings.—The majority of the fragments appeared to be united by new osteoid tissue (Figs. 2 and 3). Part of these fragments were composed of well stained tissue like regenerated bone, while other portions contained poorly stained nuclei. There were some separate fragments that were made up mostly of degenerated nuclei, only a portion on the periphery taking the nuclei stain. The marrow spaces of the major portion of the specimen were filled with a vascular fibrous marrow.

EXPERIMENT 8 (Dog 64, forty-two days).—*Operation*.—A piece of bone was removed from the femur and broken into several fragments, after which it was placed in a piece of tubing and inserted into the knee joint. The dog opened the wound on the eighth day.

Gross Findings.—The joint cavity was filled with clear synovial fluid. The tube was slightly adherent to the synovial membrane at one place. The bone appeared dead.

Microscopic Findings.—There was practically a complete failure of staining of the nuclei of the bone.

EXPERIMENT 9 (Rabbit A (2), fifty-six days).—*Operation*.—A segment of bone was removed from the metatarsal bone and after being tied in rubber tubing was inserted into the left knee joint.

Gross Findings.—The rubber tubing was found adherent to the synovial membrane. The bone appeared viable.

Microscopic Findings.—There was a large amount of cartilaginous and osseous callus connecting the fragments of bone. The nuclei of the original bone for the greater part were stainless; only those about the periphery and the haversian canals stained. The marrow spaces contained in part normal marrow cells, and in some places fat and fibrous tissue.

EXPERIMENT 10 (Dog 63, sixty-eight days).—*Operation*.—Several fragments of bone obtained from the metatarsal bone were placed in rubber tubing and dropped in the joint cavity of the right knee.

Gross Findings.—The specimen was found attached in the region of the subpatella fat pad. The bone had undergone considerable absorption.

Microscopic Findings.—The bone was well stained throughout and it appeared as though the fragments had united and that regeneration was complete. There were a number of giant cells on the surface and evidence of absorption.

EXPERIMENT 11 (Dog 65, seventy-two days).—*Operation.*—A small piece of bone, the periosteum of which was partly detached, was removed from the upper



Fig. 2 (Experiment 7, forty days).—Fragments of bone were placed in perforated rubber tubing and dropped into the knee joint. The tubing was found attached to the synovial membrane and the contained fragments were united by osteoid callus. *A-A*, original bone, showing poor staining of nuclei; *C*, new osteoid callus connecting the two fragments.

end of the right fibula. The bone was fragmented and after being placed in rubber tubing was inserted into the knee joint.

Gross Findings.—The tube was found attached on the side of the quadriceps pouch. The bone had undergone marked atrophy but appeared viable.

Microscopic Findings.—The remnant of bone was encapsulated by connective tissue. Most of the nuclei stained normally. The bone was evidently undergoing absorption, and there was no evidences of proliferation.

EXPERIMENT 12 (Dog 67, eighty days).—*Operation.*—A piece of bone 3 cm. long was removed from the left fibula and after being broken into a number of fragments was placed in rubber tubing and inserted into the knee joint of the same side.

Gross Findings.—The specimen was found attached to the joint lining. The fragments of bone appeared alive and it looked as though they were united.

Microscopic Findings.—There was a definite union of all the fragments. In the original bone the nuclei about the haversian canals and on the periphery



Fig. 3 (Experiment 7, forty days).—Area A-C shown in Figure 2 under higher magnification; A-A, poor staining of original bone; C-C, new well stained osteoid callus extending to another fragment of bone.

stained well, while some on the interior failed to stain. There was new osseous callus connecting the various fragments, and in some places it was still cartilaginous. The bone spaces contained vascular fibrous marrow.

EXPERIMENT 13 (Dog 66, eighty-eight days).—*Operation.*—A piece of bone 3 cm. long with periosteum and endosteum was removed from the upper end of the right fibula; this was fragmented and after being put in a rubber tubing was inserted into the knee joint of the same side.

Gross Findings.—The specimen was found attached in the region of the quadriceps pouch. One small piece was found in the rubber tubing and another piece was outside the tube, both having undergone considerable absorption.

Microscopic Findings.—The larger piece of the specimen was composed of two types of bone, one that appeared to be undergoing degeneration and absorption

and another that was proliferating. The marrow spaces contained both fibrous and lymphoid marrow. The smaller piece of bone contained only a few well stained nuclei and was evidently undergoing absorption.

EXPERIMENT 14 (Dog 67, one hundred and eight days).—*Operation*.—Two specimens of fragmented bone from the right fibula, after being placed in rubber tubing, were inserted into the knee joint.

Gross Findings.—Only a small fibrous nodule was found.

Microscopic Findings.—No bone was found in the section.

SUMMARY

1. In these experiments in which pieces of bone enclosed in rubber tubing were inserted into a joint, well stained or new bone was found in practically every case in which a sufficient time had elapsed. The cycle and the character of the changes were similar to those which took place in a transplanted piece of bone under normal conditions. The processes were slower, less active, and there was a tendency for earlier degeneration.

2. In some of the experiments, cartilaginous and osteoid callus was found uniting the fragments. The ultimate fate after restoration was complete absorption, as with other transplants in a nonfunctioning position.

3. After insertion in the joint cavity, the specimens more than likely remained free for several days. At eight days one was found attached to the synovial membrane, but was surrounded by unorganized fibrin. At nineteen days there was beginning organization at the place of attachment; therefore, it seems justifiable to conclude that for the period previous to this time, the fragments were able to subsist on nutrient material obtained from the synovial fluid. We should bear in mind that the fragments were enclosed in perforated rubber tubing and thereby received only a limited supply of necessary food elements; it was therefore all the more remarkable that the fragments were not only able to survive but to form callus in sufficient amount to have united the pieces of bone.

4. The foreign bodies excited no inflammatory reaction on the part of the synovial membrane, and no changes took place in the articular cartilages.

5. In every experiment the tube with its enclosed contents became adherent to the synovial membrane, thereby defeating the primary purpose of this investigation, but the results are nevertheless interesting and important. It is hoped that methods may be devised by which the fragments may be kept free in the joint cavity, or for the successful cultivation of bone outside the body.

CONCLUSIONS

1. Bone fragments placed in perforated rubber tubing and inserted into a joint remained viable and were able to produce sufficient new bone to form a union between the fragments.
2. The foreign bodies caused no injury to the articular cartilage and always became adherent to the synovial membrane.

TUBERCULOSIS OF THE MAMMARY GLAND*

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The education of the public to look on any mass in the breast as a potentially serious condition is leading to more satisfactory treatment of the neoplastic lesions of this organ. Granted, however, that every mass in the breast is to be considered malignant by the laity until proved otherwise, the physician must be able, within reasonable limits, to differentiate between the benign and the malignant new growths. Certainly tuberculosis of the breast holds a definite place among the benign conditions of this organ which must be differentiated from the malignant. The number of cases, however, remain small as compared with the number of cases of neoplasm and no one group of cases of mammary tuberculosis has been large enough in itself to allow of general statements or definite conclusions. The number of cases proved by microscopic examination and completely reported in the literature probably is now sufficient, when reviewed as a whole, to allow fairly accurate deductions.

Before the advent of microscopic section methods of examining tissues there were many who doubted the existence of tuberculous mammary gland disease, some being so bold as to state that this was the one organ exempt from this infection. Among these stood Virchow. Cooper¹ described the condition in 1829 but his experience, like that of many of the earlier observers, was limited to the more advanced and more evident type or stage of the disease, that is, cases in which well developed cold abscesses were present or those in which sinus formation had already taken place. The frequency with which less extensive forms and earlier stages of the disease are being reported is due as much, no doubt, to the education of the laity to look on any mass in the breast with grave suspicion as to the improved diagnostic methods. Greater attention must be given, then, to the differential diagnosis of early stages of tuberculosis of the breast in order to suspect such a condition.

There are certain classical notions regarding mammary gland tuberculosis, some of which are not entirely correct in view of the entire series of reported proved cases. Among these accepted statements are: (1) that the condition is rare; (2) that the disease early takes the form of abscesses and sinuses; (3) that axillary and cervical gland tuberculosis often precede the breast condition and the latter results from a

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1. Cooper, Astley: Illustrations of Diseases of the Breast, London, 1829.

lymphatic extension from these primary foci; (4) that gland involvement occurs during the period of sex activity; (5) that the process is practically always unilateral; (6) that the right breast is more frequently attacked than the left; (7) that the breast lesion is associated with other foci of tuberculous infection and therefore is secondary; (8) that previous mammary infection and trauma are common predisposing causes; (9) that breast tuberculosis is always of the bovine type.

The statement that breast tuberculosis is a clinical rarity is supported by the relatively few cases reported. However, one must not overlook the fact that since attention has been directed to the condition, reports are becoming more frequent. Delbet² in 1891 was able to compile only thirty-six cases while Gauthier³ in 1895 compiled seventy-nine cases, forty-three of which were proved tuberculosis by microscopic examination. Scudder⁴ in 1898 reported eighty-three compiled cases and in the following year Carrel⁵ increased the number to 120, although all of them were not proved by microscopic examination. Pataroni⁶ in 1907 and Durante⁷ in 1914 compiled and reported sufficient cases to bring the number to 150. In 1914 Deaver⁸ reviewed the literature and compiled the cases in the period from 1904 to 1914. With the five cases he had observed himself he was able to report seventy-seven cases in which a diagnosis had been definitely established. Since 1914 fifty cases have been reported and I am permitted to add fifteen cases compiled from the Department of Surgery at the University of Michigan Hospital.

Five of the seven cases reported by Raw⁹ were not proved tuberculosis, either by finding the tubercle bacilli or by tissue examination. Of these five cases it is quite likely that one at least was not mammary tuberculosis, but rather a cold abscess beneath the breast and secondary to tuberculosis of the shoulder joint. If we disregard the unproved cases there have been forty-five cases reported which with the additional fifteen reported herewith bring the total number reported since 1914 to sixty cases.

Although only fifteen cases can be reported from the University Hospital, it is interesting to note that the Department of Pathology files show a total of fifty-two cases of mammary tuberculosis from all

2. Delbet, quoted by Chauvin, E.: Comité méd. des Biches du Rhone, Nov. 17, 1922; Arch. franco-belges de chir. 26, 1923; Progrès méd. 38:109 (March 10) 1923.

3. Gauthier: Thèse de Bordeaux, 1895.

4. Scudder: Am. J. M. Sc. 116:75, 1898.

5. Carrel: Gaz. d. hôp., 1899, p. 1945.

6. Pataroni: Thèse de Bordeaux, no. 126, 1907.

7. Durante: Policlinico 21:139, 1914.

8. Deaver: Am. J. M. Sc. 147:157, 1914.

9. Raw, N.: Brit. M. J. 1:657 (April 12) 1924.

sources, or one case to each forty-five of malignancy. This evidence compares closely with the statement of Scott¹⁰ that there is one case of tuberculosis of the breast to fifty of cancer.

The commonly accepted opinion that the disease as seen clinically is usually in the stage of abscess and sinuses is not entirely correct. A review of the compiled cases shows that only thirty-seven of 140 cases showed sinus formation when the patients first presented themselves for examination. In only eight cases of forty-eight was a diagnosis of abscess made by clinical examination. To be sure, caseation and small abscess formation are found in a much larger proportion of cases by microscopic examination. There is undoubtedly a group of cases in which evolution is very slow and these with a smaller group that present the gross picture of infiltrating granulation tissue make up the majority of the cases. The latter sclerosing type of the disease has been very aptly called the "tuberculous pseudoneoplasm" by Chauvin.¹¹ The disease takes this peculiar form, no doubt, because of the low virulence of the organism or the greater resistance of the host. In this form spread to the axillary glands may be early and here the process may go on rapidly to caseation even though the primary breast lesion remains small and of the noncaseating type.

Contrary to the once accepted opinion mammary tuberculosis is not commonly due to spread of the infection from cervical and axillary glands. Raw⁹ stresses the secondary involvement of the breast from extensive cervical and axillary tuberculosis in five of his cases. Extension to the breast does take place in this way but much less frequently than was formerly thought. Less than half the compiled cases show any cervical or axillary involvement and a large number of the patients presenting palpable axillary glands give a definite history of having observed the enlargement of the nodes after the appearance of the mass in the breast. Not more than 5 per cent of the cases of tuberculosis of the breast arise as extensions from axillary or cervical tuberculous glands.

Only five cases of bilateral mammary gland tuberculosis have been reported, one case each by Albertin,¹² Walther,¹³ Bonneau,¹⁴ Durante and McCarty¹⁵ and Chauvin.¹¹ The disease can be considered as almost universally unilateral. There is no evidence to support the conclusion that there is a gross predilection for one breast over the other. Of 122 cases, sixty-two involved the right breast and sixty the left breast.

10. Scott: *St. Bartholomew's Hosp. Rep.* 40:97, 1904.

11. Chauvin (footnote 2).

12. Albertin, quoted by Chauvin (footnote 2).

13. Walther: *Bull. et mem. Soc. d'anat. de Paris* 32:1076, 1906.

14. Bonneau: *Société des chirurgiens de Paris*, Oct. 15, 1920.

15. Durante, L., and McCarty, W. C.: *Ann. Surg.* 63:668 (June) 1916.

Secondary involvement of the breast from a tuberculous focus elsewhere is much less common than was thought by early observers. The more usual locations for primary foci, when present, are cervical and axillary glands and the lungs. The earlier writers on the subject considered mammary tuberculosis to be secondary to pulmonary infection in all cases. At present there is a tendency to an almost complete reversal of this opinion. The truth lies in a middle ground. Scott¹⁰ in reporting twenty-seven cases found no case of pulmonary tuberculosis. In the group of sixty cases reported since 1914 (including the fifteen reported at this time) eighteen patients showed tuberculosis or gave a history of having had a definitely diagnosed tuberculous lesion elsewhere than the breast. Of these eighteen patients ten had pulmonary tuberculosis. Chauvin¹¹ places the association of the breast condition with a pulmonary infection at 12 per cent while the foregoing analysis would put the incidence at 16.6 per cent.

Trauma and previous chronic inflammation of the breast have been considered important predisposing factors. Trauma is given as a definite cause in but two cases of forty-eight and previous chronic inflammation of the breast was present in only 10 per cent of the cases. Although trauma cannot be considered a causative factor, frequently here, as in benign growths of the breast, an injury will lead to the discovery of the condition. Four cases of tuberculosis of the breast associated with benign neoplasms have been reported by Walther,¹² Schley,¹⁰ Massabuan¹⁷ and Bundschuk.¹⁸

All cases in which the type of bacillus has been determined have proved to be bovine in type, but the number of cases from which the bacilli have been cultured is much too small to warrant conclusions. The difference in the rapidity of caseation in various cases may be explained by the type of infection. It is known that elsewhere in the body the bovine infection more often runs a chronic course than does the human bacillus infection.

Attempts have been made to classify tuberculosis of the breast as disseminated or confluent but the increasing number of cases that cannot be forced into such a grouping has led to the adoption of a classification on a quite different basis. If, indeed, a classification is necessary, the following seems to answer the present needs:

Primary:

1. Breast tuberculosis with rapid evolution.
2. Breast tuberculosis with slow evolution.
3. Sclerosing type (tuberculous pseudoneoplasm).

Secondary:

Tuberculosis of breast from glandular origin; rapid evolution.

16. Schley: St. Lukes Hosp. Rep., 1910, p. 1147.

17. Massabuan: Montpel. méd. 28:608, 1909.

18. Bundschuk: Beitr. z. path. Anat. u. z. allg. Pathol. 57:65, 1913.

The more common form of the disease is that of a localized mammary gland lesion, without demonstrable focus elsewhere, with or without spread to the axillary nodes. The process here, if not interrupted by treatment, goes through three stages: nodule, abscess and sinus. The rapidity with which the change takes place varies and the subdivision of the primary group is made on this basis of rapidity of evolution of the process. Every stage is possible. Caseation may take place early with abscess and fistula formation simulating subacute mastitis or the process may be of the sclerosing type that remains for several years without breaking down.

DIAGNOSIS

The lump in the breast is insidious in its onset and usually free from pain until distention of the tissues by a considerable mass occurs or the overlying skin is involved. In twenty-three of forty-eight reported cases there was slight or severe pain at the time of the first examination but in only two had pain been an early symptom. Early abscess and sinus formation takes place in the secondary and rapidly evolving primary types (usually within two to four months). These two groups, when taken together, make up less than 20 per cent of the cases. Diagnosis in these cases is usually evident and it is not surprising that before laboratory methods of diagnosis were available these were the only known types.

The slowly caseating type along with the sclerosing form make up a most interesting clinical entity. It is this group in which diagnosis is most difficult. It is not uncommon for these patients to give a history of a lump in the breast for several years. Remissions followed by an increase in size of the mass with pregnancies or menses occur in some cases. One case (case 1) of our series gave such a history with remissions and exacerbations extending over a period of eight years. Four of the patients had first noticed the lump more than a year before admission and in none had the first symptoms appeared less than five months before the patient came for examination. In none of the cases had sinus formation occurred. Axillary gland involvement is usually relatively early, but it is of no value in differential diagnosis. Fixation and dimpling of the skin and retraction of the nipple may be present. In a case reported by Miles¹⁹ and another by Hartman and d'Allaines²⁰ retraction of the nipple was the first indication of a lesion. Discharge

19. Miles: *Edinburgh M. J.* 14:205, 1915.

20. Hartmann, Henri; and d'Allaines, G.: *Bull. Soc. d'obst. et de gynec. de Paris*, 1924, no. 6.

| Reported by Miles ¹⁹ | Year | Sex* | Age | Social | Children | Side In- | Fistula | Duration of Sym- ptoms | Size | Location in Breast | Pain | Condition of Skin | Nipple | |
|------------------------------------|------|------|-----|--------|----------|--------------|-------------------------|------------------------------|----------------------------|-----------------------------------|--|--|------------------|----------------|
| | | | | | | volv- ed | or Sinus | | | | | | Retrac- tion | Dis- charge |
| 1..... | 1915 | ♀ | 40 | S | .. | R | | | Hen's egg | Lower half | With ap- pearance of swelling + | Not ad- herent | First symptom | Milky white |
| 2..... | 1915 | ♀ | 36 | M | 9 | R | + | Several weeks | Large lump | Central | + | Dark blue over swell- ing | + | |
| 3..... | 1915 | ♀ | 47 | M | 10 | L | + 2 | About (?) 2 weeks | Large mass to axilla | Upper outer | None | Bluish about sinuses | + | |
| 4..... | 1915 | ♀ | 29 | M | 2 | L | | | | Upper inner | Not stated | Not stated | Not stated | Not stated |
| 5..... | 1915 | ♀ | 35 | M | 2 | L | + | 6 weeks | 5 by 3 in. | Upper outer | + | Bluish mov- able edges about sinuses | + | Not stated |
| 6..... | 1915 | ♀ | 23 | S | .. | R | | 4 months | Orange | Near nipple | No | Not adherent | Not stated | Not stated |
| Gatewood ²² | | | | | | | | | | | | | | |
| 1..... | 1916 | ♀ | 36 | M | 1 | R | + sev- eral | 4 years | 2 cm. in diameter | Upper inner | Slight | Not stated | + | + |
| 2..... | 1916 | ♀ | 26 | S | .. | R | + | 7 months | 3 cm. when first noted | Not stated | No | Not stated | Not stated | Not stated |
| 3..... | 1916 | ♀ | 37 | M | 6 | R | With healing 3 + | 18 years | At largest 4 cm. | Below nipple | During menses | Reddened | Not stated | Not stated |
| 4..... | 1916 | ♀ | 46 | M | 6 | L | Follow- ing incision | Indefinite period | 6 cm. | Upper inner | Slight | Numerous old scars | Not stated | Not stated |
| 5..... | 1916 | ♂ | 44 | .. | .. | L | | 6 months | Not stated | Outer | No | Not stated | Not stated | Not stated |
| Durante and McCarty ²³ | | | | | | | | | | | | | | |
| 1..... | 1916 | ♂ | 52 | .. | .. | L | Single abscess | | | Lower | Not stated | Slight in- flammation | No | Not stated |
| 2..... | 1916 | ♀ | 28 | .. | .. | L | | | | Upper outer | + | Not in- volved | No | Not stated |
| 3..... | 1916 | ♀ | 23 | .. | .. | L | Single abscess | | | Lower outer | Slight | Slight in- flammation | No | |
| 4..... | 1916 | ♀ | 27 | .. | .. | L | | | | Upper outer | Slight | Not in- volved | No | |
| 5..... | 1916 | ♀ | 40 | .. | .. | R | | | | Upper outer | Slight | Not in- volved | + | |
| 6..... | 1916 | ♀ | 26 | .. | .. | R & L | | | | Upper inner and upper outer | Slight | Not in- volved | No | |
| | 1916 | ♀ | 22 | .. | .. | L | + | | | Nipple region | Slight | Not in- volved | No | |
| 8..... | 1916 | ♀ | 41 | .. | .. | L | + 1 | | | Upper ex- terior | Slight | Ulcerated | No | |
| 9..... | 1916 | ♀ | 28 | .. | .. | R | | | | Generalized | Slight | Not in- volved | + | |
| 10..... | 1916 | ♀ | 42 | .. | .. | R | | | | Generalized | Slight | Not in- volved | No | |
| Hamilton ²³ | | | | | | | | | | | | | | |
| 1..... | 1920 | ♀ | 44 | .. | .. | R | | | | Not given | | | | |
| Cheever ²⁴ | | | | | | | | | | | | | | |
| 1..... | 1921 | ♀ | 37 | M | .. | L | | 7 months | | Upper outer | Stabbing pain | | + | |
| 2..... | 1921 | ♀ | 23 | M | .. | L | + 3 | 6 months | | Lower central | Slight + | Ulcer | | |
| 3..... | 1921 | ♀ | 21 | S | .. | L | | Not given | Mass | Not given | | Not in- volved | | |
| 4..... | 1921 | ♀ | 36 | M | .. | Not given | After inc. | 7 weeks | Mass | Not given | Tender- ness | Sinus | | |
| Archibald ²⁵ | | | | | | | | | | | | | | |
| 1..... | 1922 | ♀ | 40 | M | 1 | L | | 16 months | | Not given | + | | + | |
| Elkin ²⁵ | | | | | | | | | | | | | | |
| 1..... | 1923 | ♀ | 36 | .. | .. | R | + | Not given | | Upper inner | | Sinuses | | |
| 2..... | 1923 | ♀ | 21 | .. | .. | L | + | Not given | | Lower outer | | Sinus | | |
| 3..... | 1923 | ♀ | 26 | .. | Yes | R | | Not given | | Lower | | Not given | | |

* In this table, ♂ indicates male; ♀, female.

²² Gatewood: Mammary Tuberculosis. J. A. M. A. 67:166 (Dec. 2) 1916.²³ Hamilton, E. P.: Surg. Gynec. Obst. 30:567 (June) 1920.

| Palpable Axillary Gland | Initial Symptoms | Previous Condition of Breast | General Physical Examination | General Health | Heredity | Treatment | Result | Microscope Diagnosis | Tuber- culosis Found | Animal Inocu- lation |
|-------------------------------|--|--|--|----------------|---------------------------------|---|-------------------------------|----------------------|----------------------|----------------------|
| | Retraction of nipple | Normal | Amputation right leg, tuber- culosis knee | Good | Tuberculosis in family | Excision of breast | Satisfactory | Plus | | |
| | Lump | Abcess 3 years before | Negative | Good | Negative history | Partial excision of breast | Discharged practically healed | | | |
| + | Lump | Normal | Negative | Good | Negative history | Partial excision of breast and axillary glands | Satisfactory | | | |
| | Abcess | Incision and drainage; abcess 2 weeks; healed | Negative | Good | One sister died of tuberculosis | Incision and drainage | Slow healing | | | |
| Single nodule | Pain and lump | Retracted nipple | Negative | Fair | Negative history | Excision of breast and axillary glands | Uneventful recovery | Plus | | |
| No | Lump | Normal | Negative | Good | Negative history | Excision of portion of breast | Healed | Plus | | |
| No | Lump | | Negative | Excellent | Negative history | Abcess and sinuses removed | Primary closure | Plus | | |
| Not stated | Lump, 3 cm. | Normal | Pulmonary tuberculosis | Good | Negative history | Partial breast excision | Healed | Plus | | |
| + | Lump | Injured 18 years before; abcess, swelling and pain | Negative | Good | Negative history | Excision of breast | Primary healing | Plus | | |
| + | Lump | Numerous incisions and drainage of abcesses | Negative | Good | Negative history | Excision of breast | Not stated | Plus | | |
| Operation previously | Swelling | Normal | Lost 20 pounds (9 Kg.) in 1 year | Fair | Negative history | Excision of outer half of breast | Not stated | Plus | | |
| Not stated | | Not given | Tuberculosis of lungs; left empyema | Poor | Negative history | Not stated | Not stated | Plus | | |
| No | Single nodule | Not given | Tuberculosis of lungs | Poor | Negative history | Not stated | Not stated | Plus | | |
| No | | Not given | Tuberculosis of lungs | Poor | Tuberculosis in family | Not stated | Not stated | Plus | | |
| No | Nodular; multiple | Not given | Tuberculosis of lungs | Poor | Tuberculosis in family | Not stated | Not stated | Plus | | |
| No | Single nodule | | Negative | Good | Negative history | Not stated | Not stated | Plus | | |
| Both axillary glands | Nodular; multiple | | Tuberculosis of lungs | Poor | Negative history | Not stated | Not stated | Plus | Plus | |
| Both; neck | Cyst | | Negative | Good | Negative history | Not stated | Not stated | Plus | | |
| No | | | Negative | Good | Negative history | Not stated | Not stated | Plus | Plus | |
| Right axillary; both cervical | Diffuse sclerosis | | Negative | Excellent | Negative history | Not stated | Not stated | Plus | Plus | |
| Right axillary | Diffuse sclerosis | | Appendix and right adnexa removed; 2 years | Poor | Negative history | Not stated | Not stated | Plus | Plus | |
| + | | | Pulmonary | Not stated | Not stated | Excision of breast and axillary glands | Healed | Plus | | |
| | Lump | | Negative | Good | Negative history | Partial excision of breast and axillary | Not stated | Plus | | |
| | Mass | | Negative | Good | Negative history | Amputation of breast, gland dissection and roentgen-ray treatment | Not stated | Plus | | |
| | Mass | Negative | Negative | Good | Not stated | Partial excision of breast | Healed | Plus | | |
| | Tender mass | Negative | Negative | Good | Not stated | Excision of breast | Healed | Plus | | |
| | Painful mass subsided; returned in 3 mo. | After 12 months | Negative | Good | | Excision of breast and part of axillary gland | | Plus | | |
| + | | Negative | Negative | Good | | Amputation of breast | Healed 5 years | Plus | | |
| | | History of trauma | Negative | | | Breast amputation | Healed 1 year | Plus | | |
| | | Negative | Negative | Good | | Partial excision of breast | Healed 2 years | Plus | | |

24. Cheever, D.: Surg. Clin. N. Amer. 1: 919 (June) 1921.

25. Archibald, R. G.: Ann. Trop. Med. 16: 235 (Oct.) 1922.

26. Eikin: Ann. Surg. 77: 661 (June) 1923.

| Reported by | Year | Sex* | Age | Social | Children | Involved | Fistula or Sinus | Duration of Symptoms | Size | Location in Breast | Pain | Condition of Skin | Nipple | |
|---|----------|------|-----|--------|--------------------|-----------|-----------------------------|----------------------|-------------------------------|------------------------------|----------------|---------------------------------------|----------------|-----------|
| | | | | | | | | | | | | | Retraction | Discharge |
| 4..... | 1923 | ♀ | 24 | .. | .. | L | | Not given | | Lower inner | | Not given | | |
| 5..... | 1923 | ♀ | 23 | .. | Yes | L | + | Not given | | Lower inner | | Sinus | | |
| 6..... | 1923 | ♀ | 37 | .. | At time of onset | L | + | Not given | | Upper outer | | Sinus | | |
| 7..... | 1923 | ♀ | 34 | .. | Yes | R | + | Not given | | Central | | Sinus | | |
| Chauvin | | | | | | | | | | | | | | |
| 1..... | 1923 | ♀ | 38 | M | 1 | L | Abscess | 1 month | Nut | Nipple and outside of nipple | | Adherent later | | |
| 2..... | 1923 | ♀ | 25 | M | .. | L | Axilla | Very long | | Superior external | + | Adherent | | |
| 3..... | 1923 | ♀ | .. | M | 8 | R & L | | 16 days | | Superior external | + | | | |
| Raw | | | | | | | | | | | | | | |
| 1..... | 1924 | ♀ | 17 | S | .. | Not given | After drainage | Few weeks | | | | Sinus | | |
| 2..... | 1924 | ♀ | 37 | .. | .. | R | + | 1 year | | | | Sinuses | | |
| 3..... | 1924 | ♀ | 19 | .. | .. | R | | Not given | | | | Sinuses | | |
| 4..... | 1924 | ♀ | 33 | .. | .. | R | + | 6 years | Massive | | | Sinuses | | |
| 5..... | 1924 | ♂ | 27 | .. | .. | L | | | | | | | | |
| 6..... | 1924 | ♂ | 23 | .. | .. | L | | | | Upper | | | | |
| 7..... | 1924 | ♂ | 22 | .. | .. | R | | 2 months | | | + | | | |
| Hartmann and d'Allaines²⁰ | | | | | | | | | | | | | | |
| 1..... | 1924 | ♀ | 40 | M | .. | Not given | | | | Central | | Reddened; fixed to mass | + | |
| 2..... | 1924 | ♀ | 59 | M | .. | R | | 3 weeks | Small | | + | Adherent | | |
| 3..... | 1924 | ♀ | 25 | M | 1 miscellaneous | Not given | | 18 months | 4 nodules | Upper outer | | Slightly red-dened; slightly adherent | + | |
| | 1921 | ♀ | 24 | M | 2 | R | | 1 year | Mass | Inner upper | + | Reddened | + | + |
| Diversity Hospital | | | | | | | | | | | | | | |
| 1..... | 10/13/17 | ♀ | 30 | M | 3, 1 miscellaneous | R | After incision and drainage | 8 years at intervals | Hen's egg | Outer | + | Sinuses | + | + |
| 2..... | 5/ 1/19 | ♀ | 38 | M | .. | R | | 18 months | Small | Inner outer | + | | | |
| 3..... | 7/18/22 | ♀ | 47 | M | 6 | R | | 9 months | Pigeon's egg | Center | | | | |
| 4..... | 12/ 4/22 | ♀ | 43 | M | .. | R | | 5 months | Mass | | + | | | |
| 5..... | 1/26/25 | ♀ | 47 | M | 12 | L | | 16 months | 3 by 5 in. | Upper outer | | | Slight | |
| 6..... | .. | ♀ | 40 | M | 5 | R & L | | 7 weeks | Small mass | Central | + | | Slight on left | |
| 7..... | .. | ♀ | 29 | M | 2 | R | | 6 months | Large mass | Outer | Slight | | | |
| 8..... | 11/22/12 | ♀ | 34 | M | 3 | L | | 17 months | Mass sub-sided and reappeared | Outer | Slight | | | |
| 9..... | .. | ♀ | 50 | M | 4 | L | | | Hen's egg | Outer | Slight | | | |
| 10..... | .. | ♀ | 22 | S | .. | R | | 5 months | Cherry | Upper outer | | | | |
| 11..... | .. | ♀ | 27 | M | . | L | | 5 months | Lump | Above nipple | | | + | |
| 12..... | .. | ♀ | 32 | M | 4 | R | | 14 years | Hickory-nut | Upper outer | Present 1 year | Scar | + | |
| 13..... | .. | ♀ | 30 | M | 2 | R | | | Lump | Upper | | | | |
| 14..... | .. | ♀ | 22 | M | .. | L | | 5 months | Mass | Lower | Slight | Fixed | | |
| 15..... | .. | ♀ | 29 | M | 3 | R | | 6 months | Mass | | Slight | | + | |

* In this table, ♂ indicates male; ♀, female.

Cases—Continued

| Palpable Axillary Gland | Initial Symptoms | Previous Condition of Breast | General Physical Examination | General Health | Heredity | Treatment | Result | Microscopic Diagnosis | Tuberculosis Found | Animal Inoculation |
|-------------------------|-----------------------|---|---------------------------------------|----------------|--------------------------|--|--------------------------------|-------------------------|--------------------|--------------------|
| + | | Negative | Tuberculosis of rib | | Tuberculosis in family | Excision of sinus and rib | Healed 5 years | Plus | | |
| + | | Negative | Negative | | Negative history | Breast amputation; dissection of axilla | Well, 18 months | Plus | | |
| | | Negative | Negative | | Negative history | Partial breast amputation | Well, 3 months | Plus | | |
| | | Negative | Tuberculosis of lung | | Negative history | Breast amputation | Well, 5 months | Plus | | |
| | Nodule | Negative | Negative | Good | Negative history | Partial excision of breast | Healed 1 year | Plus | | Plus |
| + | Small nodules | | Suspected tuberculosis | Fair | Negative history | Partial breast amputation and axillary dissection | Healed | Plus | | |
| + | Mass | | Lung | Poor | Negative history | Amputation of breast and axillary dissection | Healed | Plus | | |
| Cervical; axillary | Mass | Negative | External cervical tuberculosis | | | Drainage of abscess | Healed, 10 months | | Bovine | |
| Axillary; cervical | Mass | Negative | External cervical and axillary | | | None | Not known | | Bovine | |
| Axillary; cervical | | Negative | External tuberculosis of gland | | | Sinuses scraped | Healed, 16 months | | | |
| Cervical | Mass | | External cervical tuberculosis | | | Sinuses scraped | Healed, 11 months | | | |
| | | Tuberculosis of axillary glands; shoulder | | | | | | | | |
| Cervical and axillary | Mass | Negative | | | | Of cervical and axillary sinuses | Breast subsided | | | |
| | Mass fluctuation | | Tuberculosis of knee, ankle and tibia | | | General hygienic | | Not proved tuberculosis | | |
| One axilla | Retraction of nipple | Negative | Negative | Good | Negative history | Amputation of breast, axillary dissection | Healed, 1 year | Plus | | |
| Axilla + | Pain nodule | Negative | Negative | Good | Tuberculous history | Breast amputation; axillary dissection | Healed, 9 years | Plus | | |
| Axilla and supra-axilla | Nodule | Negative | Negative | Good | Negative history | Radical breast amputation | Healed | Plus | | |
| Axilla | Discharge from nipple | Negative | Negative | Good | Negative history | Incision and drainage of abscess | Healed | | | Tuberculosis found |
| Axilla | Swelling and pain | Negative | Negative | Fair | Negative history | Breast amputation; axillary dissection | Healed | Plus | | |
| Axilla | Mass | Negative | Negative | Good | Negative history | Incision and drainage | Wound draining when discharged | Plus | | |
| | Mass | Negative | Negative | Poor | Negative history | Radical breast amputation | Healed | Plus | | |
| | Pain and mass | Negative | Enlarged spleen | Good | Negative history | Radical breast amputation | Healed | Plus | | |
| | Mass | Abscess 16 years before | Negative | Fair | Husband had tuberculosis | Local excision of masses; later, breast amputation | Healed | Plus | | |
| | Pain | Negative | Negative | Good | Negative history | Radical breast amputation | Healed | Plus | | |
| + | Mass | Negative | Negative | Good | Negative history | Amputation of breast | Healed | Plus | | |
| | Mass and pain | Negative | Negative | Good | Negative history | Amputation of breast | Healed | Plus | | |
| | Mass | Negative | Negative | Good | Negative history | Partial excision of breast | Healed | Plus | | |
| | Mass | Negative | Negative | Good | Negative history | Local excision of mass | Healed | Plus | | |
| | Retraction of nipple | Negative | Negative | Good | Negative history | Amputation of breast | Healed | Plus | | |
| | Mass | Mass 14 years | Negative | Fair | Negative history | Amputation of breast | Healed | Plus | | |
| + | Mass | Negative | Negative | Good | Negative history | Amputation of breast | Healed | Plus | | |
| | Mass | Negative | Negative | Fair | | Local excision of mass | Healed | Plus | | |
| | Mass | Negative | Negative | Good | Negative history | Amputation of breast | Healed | Plus | | |

from the nipple is an uncommon finding but attracted attention to the condition in a case observed by Hartman and d'Allaines.²⁰ Pain was the primary symptom in five of forty-eight cases.

On palpating the breast it is found that the slowly evolving forms do not present a well defined border as do the more rapidly caseating types, here again presenting the characteristic findings of a scirrhus carcinoma. Large portions or the entire breast may be involved with a diffuse sclerosis, making the involved breast more prominent and firmer than normal.

The age of the patient (tuberculosis of the breast occurs more often in younger persons than does cancer) along with a history of remissions can only suggest the correct diagnosis. Confirmation must always come from tissue examination.

TREATMENT

Opinion unanimously favors surgical treatment. If there is a well localized lesion in the breast this may be removed along with a margin of normal tissue; if the process is more extensive, the entire breast must be removed along with the axillary glands when definitely involved. It is not necessary to take as wide a margin of skin as in cancer and the pectoral muscles can be saved in the majority of cases. Removal of the outer portion of the pectoralis major may be necessary in order more easily to attack the axilla. Primary healing is the rule, recurrence uncommon.

With more conservative treatment such as the medical treatment as advocated by Von Eberts,²¹ the results are quite unsatisfactory. More conservative operative measures, such as draining of abscesses and curettement of sinus tracts and iodoform gauze dressings, have given local healing but only after months of treatment. Recurrence after the more consecutive forms of treatment is much more common.

CONCLUSIONS

1. Tuberculosis of the breast occurs in the proportion of 1:40 as compared with cancer of the breast and 1:20 with other chronic inflammations of the breast.
2. In the majority of cases, no other tuberculous lesions can be found.
3. Sclerosing and slowly evolving types are clinically difficult to diagnose and can only be suspected.
4. Local excision of the lesion or breast amputation with removal of the axillary glands, if these are palpable, is the treatment of choice.
5. The pectoralis muscles can be preserved in the majority of cases.

21. Von Eberts: *Am. J. M. Sc.* 138:70, 1909.

THIRTIETH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY *

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CONGENITAL CONDITIONS

Congenital Dislocation of the Patella.—Zanoli¹ gives an interesting study of congenital dislocations of the patella. He has observed and studied thirteen patients, forming a total of sixteen cases. The cases may be divided into two classes, permanent dislocations and habitual dislocations. He has made a study of the literature and discusses it and also various operations that have been devised. His article is illustrated by excellent photographs and roentgenograms. As regards etiology, heredity seemed frequently to be a factor. There was also a familial factor, since he noted in the literature one instance in which three sisters had the same deformity. Sex played no part. The pathology is obscure, but his conclusion is that congenital dislocation of the patella is due to an abnormal orientation of the articular axes and more precisely to an external rotation of the tibia and an inward torsion of the distal epiphysis of the femur. Certainly the essential cause is some intra-uterine mechanical factor. He discusses the various methods of treatment that have been employed. In his series of cases various methods were used, and in regard to them he says, "I believe I do not err in asserting that the methods which merit a greater appreciation and a larger application are medial transplantation of the patellar tendon and capsulorrhaphy, which can, with much advantage, be combined."

Congenital Elevation of the Scapula.—Schrock² states that in an embryo of five weeks the scapula becomes differentiated opposite the fourth, fifth and sixth cervical vertebrae; at the ninth week the scapula begins to descend from the neck to the thorax. Failure to descend gives

* This Report of Progress is based on a review of 186 articles selected from 412 titles dealing with orthopedic surgery appearing in medical literature between Dec. 12, 1925, and March 13, 1926. Only papers that seem to represent progress have been selected for note and comment.

1. Zanoli, R.: *Chir. d. org. di movimento* 10:83 (Dec.) 1925.

2. Schrock, R. D.: *J. Bone & Joint Surg.* 8:207 (Jan.) 1926.

rise to the deformity. This failure may be due to maldevelopment in bone, cartilage and muscle, or the descent may be interrupted by abnormal pressure or position in utero. He describes a very radical procedure that has given good results in two severe cases. He believes that the complete correction of the bony deformity often necessitates such operation. The incision is curved from the midsuprascapular region from about 1 inch (2.5 cm.) external to the medial margin of the scapula to 2 inches (5 cm.) below the inferior angle. The deeper incision is carried through the cartilaginous medial margin of the scapula with subperiosteal removal of the combined attachments of rhomboids, serratus magnus and subscapularis. The subscapularis is completely removed. Similar subperiosteal elevation is made of the infraspinatus, teres major and minor, completely freeing the inferior angle and lower two thirds of the axillary border. The same procedure is applied to the insertion of the trapezius on the spine, to the supraspinatus, and to the structures of the superior margin of the scapula, using special care at the suprascapular notch. This is the only point at which there is danger to nerve or vessel of any consequence. The chondro-osseous bridge from the vertebrae to the superomedial margin of the scapula is removed as completely as possible; the margins of the scapula are freely removed; the supraspinatus portion is resected and much of the spine, if this is at all prominent. If the shoulder then cannot be brought back freely, an osteotomy of the base of the acromion is done. This gives a very appreciable downward and backward drop of the shoulder. One strut of the shoulder suspension has in this way been removed. The inferior angle of the scapula is anchored with heavy chromic catgut to the lowest rib possible. The dressing is with a pressure pad over the shoulder and long adhesive extending well down on to the trunk. This is a very important detail, and considerable downward and backward pressure can be applied in this manner. Over this is placed a figure-of-eight of the shoulders, such as is commonly used in fracture of the clavicle.

[ED. NOTE.—In our experience operations for the relief of congenital elevation of the scapula have often somewhat improved the condition, but never either cosmetically or functionally represented complete correction. This is certainly a very radical and extensive procedure that Schrock proposes and the end-results that he presents in roentgenograms and photographs are extremely good.]

RICKETS; BONE DISEASE OF UNCERTAIN ORIGIN

Experimental Rickets.—Buschke and Peiser³ have fed rats a substance called thallium, with establishment of the bone changes recog-

3. Buschke and Peiser, N.: *Klin. Wchnschr.* 3, 1925.

nized as rickets as it appears in rats, also the checking of growth and development, disturbance of sexual function, loss of hair, cataracts and stomach changes. Buschke and Peiser believe that thallium acts as a poison to the endocrine glands and the nervous system and that as a conclusion it seems probable that rickets is produced in the same way in human beings, i. e., that poor hygienic conditions and poor nutrition produce endocrine gland disturbance with rickets as a result.

Coxa Vara.—Noble and Hauser ⁴ have grouped seventy-five cases of coxa vara, dividing them into fifty-eight adolescent and seventeen congenital, believing that coxa vara may be so grouped. Of the fifty-eight adolescent patients, forty-two were males and sixteen females; the origin of the disease was probably some embryonic vascular disturbance of the femoral neck. In its mildest form this deformity begins at the fourth year and steadily progresses with growth. Roentgenograms will frequently show a fissure in the femoral neck in these cases. The adolescent type of coxa vara is generally seen in the obese or pituitary type of person and is noticed as a rule at the age of puberty when the adiposity is greatest. The authors believe that the pituitary gland plays an important rôle in coxa vara, trauma exerting only a minor influence.

Epiphyseal Coxa Vara.—Key ⁵ reports twenty-four cases of coxa vara and discusses at length the pathology of this condition. He believes that the true pathology is not known because no early specimen has been studied. He discusses the various theories as to etiology, and concludes that a weakness of unknown origin takes place in the periosteum which binds the head to the neck of the femur. This weakness develops at the period of most rapid bone growth. Key's review is a most extensive and exhaustive one.

[ED. NOTE.—We would suggest that as various clinical entities become defined we adopt more descriptive terms. For instance, the etiology of adolescent coxa vara is still in question, but the pathology of the condition is well known and represents a displacement of the upper epiphysis of the femur. It represents a clinical entity, and as such should be differentiated from other types of coxa vara. We would suggest the term "epiphysolysis" to designate the condition.]

Von Recklinghausen's Bone Disease.—Guillain ⁶ calls attention to the fact that two symptoms characterized the case reported by him of von Recklinghausen's disease. Extreme pain was present as the bone tumor

4. Noble, T. P., and Hauser, E. D.: Acute Bone Atrophy, Arch. Surg. 12:501 (Feb.) 1926.

5. Key, J. A.: J. Bone & Joint Surg. 8:53 (Jan.) 1926.

6. Guillain, G.: Bull. et mém. Soc. méd. d. hôp. de Paris 49:1607 (Dec. 18) 1925.

developed, disappearing afterward, and there was increased local temperature over the affected areas of bone.

Bone Lesions in von Recklinghausen's Disease.—Babonneix, Touraine and Pollet⁷ describe the deformities in certain cases of osteitis fibrosa hyperplastica as that of kyphoscoliosis so marked in character that the third lumbar body was seen in profile in an anteroposterior roentgenogram of the spine. The profile skull plate showed a hypertrophy of the bone but no change in the sella turcica. Microscopically and macroscopically the bone lesions were those of osteomalacia.

Gaucher's Disease, Showing Bone Disintegration and Joint Involvement.—Cushing and Stout⁸ report a case of Gaucher's disease in which there was marked destruction of the head and neck of the femur. There were also large collections of spleen cells (Gaucher's cells) in the bone marrow of the femoral head and neck, which were apparently the cause of the bone destruction. Gaucher's disease is a primary idiopathic hypertrophy of the spleen, with anemia, bronzing of the skin, and bleeding of the gums.

POLIOMYELITIS

The time interval between infantile paralysis cases in 253 families has been studied by Aycocck and Eaton.⁹ The period of incubation in man varies from ten to eighteen days, averaging fourteen days. It was inferred that the time of greatest infectiousness of infantile paralysis is probably at the beginning or within the first three or four days of the acute stage of the disease. This study suggests that the search for the source of infection should be centered at about the fourteenth day before the onset of acute symptoms. Making a comparative study of measles, they point out that secondary cases of measles usually occur from ten to twelve days after the onset of the initial case in the family, and that third cases occur, as a rule, simultaneously with the second cases. Infantile paralysis when introduced into a family acts quite differently from measles or scarlet fever. Only exceptionally do multiple cases occur. When multiple cases do occur, it is usually within a short time of each other, indicating simultaneous infection. The virus of infantile paralysis enters the family in such a way that in a few instances in which more than one member is affected, this is accomplished practically simultaneously.

7. Babonneix, L.; Touraine, and Pollet, L.: Bull. et mém. Soc. méd. d. hôp. de Paris 49:1601 (Dec. 18) 1925.

8. Cushing, E. H., and Stout, A. P.: Gaucher's Disease, Arch. Surg. 12:539 (Feb.) 1926.

9. Aycocck, G. F., and Eaton, P.: Am. J. Hygiene 5:724 (Nov.) 1925.

Bulbar Poliomyelitis.—McEachern¹⁰ reports six cases of what he calls epidemic bulbar poliomyelitis. All cases presented the common clinical symptom of paralysis of the muscles of the upper respiratory tract without coincident paralysis elsewhere. In several cases there was a white frothy mucus in the nose and throat. All patients were very ill and two died. The constant involvement of the muscles supplied by the eleventh nerve was unusual.

Gill,¹¹ in reviewing the symptomatology of various epidemics of poliomyelitis, found that rigidity of the neck was a symptom in 80 per cent of the cases. This is not a voluntary rigidity.

Boehm¹² discusses those cases of infantile paralysis in which most of the muscles of the leg are paralyzed and weight bearing therefore very difficult or even impossible. Boehm does not favor arthrodesis of the knee or hip in children and believes that the most important factor is proper statics. A good artificial leg allows proper weight bearing without muscular action. The paralyzed leg may also be fitted for weight bearing if the statics are correct. Any contracture of the knee or the hip must be corrected. An osteotomy in one or more places will accomplish this and the effect is what he calls a passive security. A line is drawn from the center of the hip to the front of the ankle joint. The trochanter and especially the knee must lie behind that line. Ordinarily the osteotomy is best performed above the knee, but this depends on the kind of deformity.

TUBERCULOSIS

Arthrodesis of the Sacro-Iliac Joint for Tuberculosis; Study of End-Results.—Smith-Petersen and Rogers¹³ report the present results in thirteen cases of sacro-iliac tuberculosis in which operations were performed after the method of Smith-Petersen in the last seven years. With careful examination to localize the lesion, with a well planned and correctly executed operation and with proper after-care, this lesion may thus be successfully treated. Of the thirteen patients nine are now well. There was no operative mortality. Four died of tuberculosis elsewhere in the body after periods of one and a half to two years.

[ED. NOTE.—In view of the poor prognosis that is generally assigned to this condition in textbooks, the high percentage of successful results here reported seems to us to represent real progress in the treatment of tuberculosis of the sacro-iliac joint.]

10. McEachern, John: Epidemic Bulbar Poliomyelitis, J. A. M. A. 86:90 (Jan. 9) 1926.

11. Gill, J. M.: Brit. M. J. 1:232 (Feb. 6) 1926.

12. Boehm, M.: Deutsche med. Wchnschr. 51:942 (June 5); 987 (June 12) 1925.

13. Smith-Petersen, M. N., and Rogers, W. A.: Arthrodesis for Tuberculosis of Sacro-Iliac Joint; Study of End-Results, J. A. M. A. 86:26 (Jan. 2) 1926.

Resection of the Knee for Tuberculosis in Adults.—Fredet¹⁴ reports twenty-seven cases, of which three of the patients were from 17 to 19 years, twenty were from 21 to 36, one was 51, and another 61. Of these twenty-seven patients he saw eight after four years or longer. The time at which he saw the others varied from three years to six months after operation. He obtained ankylosis in good position in all cases. Function was good in all cases, and the greatest amount of shortening was 5.5 cm. In these cases Fredet has used a metal suture to secure bony apposition without inconvenience in the majority of cases.

Iodized Oil in the Treatment of Surgical Tuberculosis.—Delbet¹⁵ reports the results of treatment by the Finikoff method, using iodized vegetable oil. The cases reported were treated under the personal direction of Finikoff and were fourteen in number; the injections were given throughout a period of from six to eight months, at five to seven day intervals. The first injection contained 10 cc. of the oil, the following 20 cc. The injections were given at points distant from the lesion. Calcium chloride was given at the same time by mouth. In cases of tuberculous abscess, multiple fistulas and tuberculous arthritis, he reports clinical cures and what seemed inevitable amputation was averted in several of these. The basic idea of the treatment known as Finikoff's is to increase the lipolytic power of the mononuclear cells, at the same time increasing the proteolytic power of the polymorphonuclear cells.

[ED. NOTE.—There are so many pitfalls to accurate observation in the estimation of results of therapy that we feel that a much larger series of cases will have to be reported before an expression of opinion is possible on Finikoff's method. To anyone attracted to the method, we would suggest the necessity of proving tuberculosis present before reporting on its cure.]

ARTHRITIS

The Orthopedic Aspects of Chronic Arthritis.—Osgood,¹⁶ in the Hugh Owen Thomas Lecture of 1925, reviews the orthopedic aspects of chronic arthritis, discussing the classification, the theories of etiology and the methods of treatment. He believes that many types of organisms and many other factors enter into the etiology of the so-called proliferative infectious or rheumatoid arthritis, Ely's type I. Complete recovery in the early stages may occur if these factors can be eliminated. In later stages arrest of the disease and functional improvement may be attained. The simple surgical removal of a focus of infection will rarely be successful in checking the progress if subsequent attention is

14. Fredet, Pierre: Bull. et mém. Soc. nat. de chir. 52:43 (Jan. 23) 1926.

15. Delbet, P.: Bull. Acad. de méd. 94:1083 (Dec. 1) 1925.

16. Osgood, R. B.: J. Bone and Joint Surg. 8:1 (Jan.) 1926.

not paid to normal bodily mechanics and the principles of better general health. The degenerative, hypertrophic form or osteoarthritis, Ely's type II, may often be present without any demonstrable cause. In its early stages if a faulty body chemistry and a faulty bodily mechanics can be corrected and intra-articular friction can be eliminated, almost complete relief from its symptoms is possible. Later, intelligent physiotherapy, protective apparatus and proper orthopedic surgery will be beneficial.

Chronic Arthritis and Diabetes.—Pemberton noted that patients with chronic arthritis seemed to improve when they were given diets low in carbohydrates and were made worse by diets high in carbohydrate. From this he concluded that patients with diabetes should be comparatively free from arthritis, because of the fact that their disturbed metabolism of sugar demanded prolonged diets low in carbohydrates. Schmitt and Adams¹⁷ observed during the last year at the Mayo Clinic 474 patients with diabetes. Fifty-one of these (10.8 per cent), who had well defined but as a rule comparatively mild diabetes, had arthritis. No noticeable improvement in arthritic symptoms occurred in consequence of the low carbohydrate regimen necessary in the presence of diabetes.

[ED. NOTE.—Although Pemberton did not differentiate between the two main types of chronic arthritis, the authors state that most of their cases were of the hypertrophic type, usually situated in the joints of the spine. They do not state how long it had existed before the diabetic diet was begun, but presumably for many years. Such a diet would in our opinion be expected to exert little favorable influence on this type II hypertrophic or osteoarthritic senile form. In fact, it might well by its high protein content aggravate it.]

The Dangers of Protein Therapy.—Treatment with protein bodies is administered to such an extent in chronic disease of the joints that it is timely for Zimmer and Buschmann¹⁸ to warn us against certain dangers in this treatment. Such dangers are the anaphylactic shock, serum disease and chronic protein poisoning. Intravenous injection is more dangerous than intramuscular injection. The injection should not be repeated at too short intervals. Changing the substance to be injected, slowly increasing the quantity, and gradual or divided injection are measures of safety. In order to avoid chronic protein poisoning, treatment should not be administered for more than four or six weeks without intermission.

17. Schmitt, E. O. G., and Adams, S. F.: Association Between Diabetes Mellitus and Chronic Infectious Arthritis. *J. A. M. A.* 86:535 (Feb. 20) 1926.

18. Zimmer and Buschmann: *Ztschr. f. ärztl. Fortbild.* 22:513, 1925.

Spondylitis and Spotted Fever.—Holst¹⁹ reports his extensive experience with spondylitis following spotted and recurrent fever. He has seen fifty-six cases. The affection begins with very sudden and rapidly increasing pain, which generally decreases even without treatment. Occasionally traumatism marks the beginning. The pain frequently radiates downward. Contracture of the legs, paresis and even paralysis may ensue, and deformities of the spine, such as kyphosis or scoliosis. In most of his cases the lumbar vertebrae were affected. The roentgenogram showed a narrowing of the intervertebral disk, changes of the vertebra itself, and the formation of bony bridging osteophytes. In some cases a complete union of two vertebrae had taken place. The clinical picture as well as the roentgenogram corresponded closely to that of spondylitis following typhoid fever, but was very different from tuberculous disease of the spine. The disease consists evidently in an osteomyelitic process which soon passes the bony limits and affects the cartilage and the perivertebral tissue. The process is generally benign and the prognosis is good. The treatment is simple and consists of rest in bed in the prone position.

BONE AND JOINT SURGERY

Ganglions.—Kuettner and Hertel²⁰ regard a ganglion as a neoplasm originating from the primitive connective tissue cells from which the joint develops. Since there is a symmetrical bilateral distribution of the tumors in 3 per cent of the cases they believe that hereditary factors play a certain part. Ganglion of the wrist is most frequent, about 80 per cent of all cases, and of these 70 per cent are seen in females of from 10 to 25 years of age who use their wrists very actively, as in piano playing or similar occupations. Ganglion of the knee or of the foot is most frequent among men after the thirtieth year. Traumatism may favor the development of the tumor, but is not considered the cause. The suggestion that tuberculosis plays a part, as is claimed by certain French writers, is not proved according to the authors. A ganglion of the flexor tendons of the fingers may produce the picture of "snapping" or "trigger finger." The differential diagnosis between a ganglion and a bursitis may be quite difficult. Spontaneous healing has been observed in about 16 per cent of the cases. Treatment may be by crushing, by subcutaneous incision and evacuation, or by complete excision. Even with the latter method, recurrence is seen in about 30 per cent of the cases.

End-Results of Treatment of Joint Wounds by Early Mobilization.—Willems²¹ has recently reexamined a number of patients with old joint

19. Von Holst, L.: *Ztschr. f. orthop. Chir.* 46:321, 1925.

20. Kuettner, H., and Hertel, E.: *Ergebn. d. Chir. u. Orthop.* 18:377, 1925.

21. Willems, C.: *Bull. de l'Acad. roy. de méd.* 5:284, 1925.

injury from gunshot wounds, which he had treated seven or eight years previously by his well known method of immediate active mobilization. He describes the ultimate results in fifteen cases of wounds of the knee and in five cases of wounds of the elbow. Most of the wounds were the result of shell explosions and in five there had been purulent arthritis. In the latter group numerous osteophytes have developed, but in none do they interfere with function. He describes the musculature as excellent in these as well as in all other cases, and he feels that the end-results bear out all his claims for the benefits of the method.

Behavior of Sequestrums in Chronic Osteomyelitis.—Van Dessel²² has made a series of experiments on rabbits which show that in the presence of infection completely separated sequestrums never unite to the newly formed involucrum or to the old bone. The zone of demarcation between the sequestrum and the involucrum, dead or alive, persists until the sequestrum completely disappears either by expulsion or absorption.

Bone Grafting of the Mandible.—Billington and Round²³ have made a report of their experience in the treatment of 2,000 cases of wounds of the jaws and face. Of these a large percentage were compound fractures of the mandible. In these the goal was to obtain osseous union, with accurate occlusion of the teeth, and at the same time avoid disfigurement. If the loss of bone was less than one-half inch (1.2 cm.) the attempt was usually made to secure contact of the fragments at the sacrifice of bony length; if more than one-half inch, it was considered necessary to employ a bone graft. In all, seventy-five patients were successfully treated by bone grafts, the defect varying from one-half inch to 5 inches (12.7 cm.). The longest graft used was 7 inches (17.7 cm.). Some of their observations are as follows: The mandible is peculiarly intolerant of foreign bodies such as wire, pegs or plates. Dovetailing of the grafts did not prove a successful method. The usefulness of the pedicle bone graft was very limited and free grafts were used almost entirely. They employed bone from various sites, but finally concluded that the ribs were too soft, the tibia too hard and too liable to necrosis, and that the best material for transplantation was the crest of the ilium which was tough and could be shaped. Splints were not used until after the wound had healed; if used earlier they caused necrosis. Their procedure was as follows: 1. Operation was not performed until all mouth sinuses were healed and all sepsis eliminated. 2. No splints were used until two weeks after the operation. 3. The operation ought not to open into the mouth, and if this accident occurred the operation was

22. Van Dessel, Arthur: J. Bone & Joint Surg., January, 1926, p. 194.

23. Billington, William, and Round, Harold: Brit. J. Surg. 13:497 (Jan.) 1926.

abandoned. 4. The graft was taken from the crest of the ilium, and the ends bevelled to fit over the bevelled ends of the mandibular fragments. It was placed with enough overlap to allow for future widening of the jaw with splints. 5. Firm bony union was usually obtained in from two to four months. 6. Prosthetic apparatus was not fitted until the end of six months.

Dupuytren's Contracture.—Under the title of Hereditary Contraction of the Palmar Fascia, Apert²⁴ reports observation of a family with Dupuytren's contraction in four generations. It affected males only, and in each successive generation it appeared at a slightly earlier age. The possibility of lead poisoning had been eliminated and thus an hereditary predisposition seemed to be the sole cause. One of the cases was treated by the application of radium emanations to the palm of the hand on five successive nights. The result was excellent; the contracted fascial bands relaxed, leaving only a cord, which does not interfere with the use of the hand.

Surgical Exposure of the Entire Radius.—Henry²⁵ describes an anterolateral incision by means of which the radius may be exposed throughout its entire length. With the hand supinated and the elbow extended, a straight incision is made extending from a point at the outer edge of the biceps belly to the tip of the radial styloid. Then the biceps tendon is exposed and the finger inserted in the muscular groove to the outer side of this tendon and passed distally to the elbow until the recurrent vascular loop is encountered. This should be ligated and divided. Then the three long muscles at the outer border of the forearm are mobilized. The tendon of the brachioradialis is detached. The elbow should be flexed 90 degrees and the supinator muscle exposed, turning it outward with the posterior interosseous nerve. The hand is pronated and the entire radius revolves into view.

Snapping or Trigger Finger.—Kroh²⁶ has made a careful study of fourteen cases of so-called "snapping" or "trigger" finger, and concludes that the cause is a stenosing tendovaginitis of the flexor tendons of the fingers. The lesion has its seat not at the region of the interphalangeal joint, as is commonly supposed, but at the level of the metacarpophalangeal joint, where the tendon sheath is physiologically narrowed by the ligamenta accessoria volaria. The snapping may occur in flexion or in extension, or in both movements. It may be caused by various changes, such as a circumscribed thickening of the tendon while the sheath is intact, or by a thickening of the sheath while the tendon is unaltered. In the latter case there may be pain on movement

24. Apert, E.: Bull. et mém. Soc. méd. d. hôp. de Paris 49:1502, 1925.

25. Henry, A. K.: Brit. J. Surg. 13:506 (Jan.) 1926.

26. Kroh, F. R.: Arch. f. klin. Chir. 136:240, 1925.

without the phenomenon of snapping. The treatment consists in the excision of the volar part of that section of the tendon sheath which interferes with movement of the tendon. Histologic examination of the tissues removed at operation showed hyperplasia of all the elements of the sheath, and if the condition was advanced there was noted laceration and vascularization of the ligaments and even hyaline degeneration. There was never any increase in the amount of fluid in the sheath, but rather a little dryness.

Arthrodesis of the Sacro-Iliac Joint for Arthritis, Traumatic or Nontraumatic.—Smith-Petersen and Rogers²⁷ have made a careful and detailed study of a group of cases diagnosed as arthritis, traumatic or nontraumatic, of the sacro-iliac joint, and which were treated by arthrodesis by the method devised by the first author. The cases of tuberculous arthritis in which similar treatments have been given are reported in a separate article which is abstracted elsewhere in this Report of Progress. The diagnosis was based on the history of pain in the region of the sacro-iliac joint and pain radiation in the leg over the area supplied by the first and second sacral nerves (posterior surface of the thigh and outer side of the calf), on the physical examination with demonstration of list of the spine to the opposite side, tenderness over the posterior sacro-iliac ligaments, limitation of movement and production of pain on raising the leg with the knee extended, demonstration of tenderness over the sacro-iliac joint by rectal examination, and on the roentgen-ray examination, which in certain cases showed pubic disalignment or actual arthritic changes in the joint and in others merely a widened joint space. There were twenty-six cases in the group. The operation has been previously described, but briefly consists in exposing the outer surface of the ilium by turning down a muscle flap in the gluteal region and then cutting a window through into the joint. The cartilage is removed and the bone plug which was removed from the ilium is then replaced and driven inward until countersunk in the sacrum. There was no operative mortality. End-results are given in twenty-six cases. Of these, twenty-three patients were completely relieved of pain. Of the three remaining patients, two complained of persistence of pain in the calf of the leg, but stated that this was far less severe than formerly and was decreasing. They have resumed their former occupations in full. The third patient showed a traumatic arthritis of both sacro-iliac joints. One side was operated on and relief of pain resulted, but there was still local and radiation pain present on the other side. Seven of the twenty-six cases have shown a stiffness in either the calf or hamstring muscles or both for varying periods of from two to six months after operation.

27. Smith-Petersen, M. N., and Rogers, William: *J. Bone & Joint Surg.* 8:118 (Jan.) 1926.

Two of the twenty-six cases are reported as failures and two as partial failures.

[ED. NOTE.—The authors of this article are to be congratulated on the thoroughness of their study and the critical attitude that they have maintained. The Smith-Petersen operation represents a distinct advance over other methods of securing ankylosis of the sacro-iliac joint, and the high percentage of successful results reported by the authors speaks for the care with which they have selected their cases. For others, however, a word of caution is necessary. The indications for operation in cases of so-called sacro-iliac strain or relaxation are by no means clear, nor even among the orthopedic surgeons is there unanimity of opinion as to what constitutes the sacro-iliac syndrome. Ill advised surgery in cases in which the patient might be made well by properly managed nonoperative treatment or in cases that have been diagnosed erroneously will not advance the cause of orthopedic surgery and only tends to cast discredit on the operation. Until more definite knowledge has been obtained on these points the operation should be employed with discretion only in carefully studied and controlled cases, and the end-results should be compiled and reported. It is important to point out that the cases here reported were all chronic cases.]

Lack of Functional Gain Following Osteotomy of the Hip.—Chlumsky²⁸ has noticed that in certain cases of old hip joint disease with ankylosis in positions of deformity, functional improvement following osteotomy to correct the deformity frequently does not take place; in fact, the gait may be worse than before the operation. This is due, according to Chlumsky, to the adaptation to the deformity which the body has undergone during the years when it was present. Relaxation of the ligaments of the knee and genu valgum is an example of such a process. After correction of the position of the hip the instability of the knee now becomes apparent, whereas before it caused no trouble. Static scoliosis with sinking of the pelvis is another factor. Long standing deformities in elderly people should therefore be approached with caution.

The Rôle of the Tensor Fasciae Femoris in Producing Deformity.—Yount²⁹ believes that the tensor fasciae femoris plays an important part in the production of deformities of the leg. Its contraction causes permanent flexion of the hip and by its pull through the iliotibial band it leads to knee flexion, knock-knee, and outward rotation of the lower leg. Subcutaneous fasciotomy of the iliotibial band has in his hands been of marked benefit in securing simultaneous correction of the hip flexion and

28. Chlumsky, V.: Zentralbl. f. Chir. 52:2298 (Oct. 10) 1925.

29. Yount, C. C.: J. Bone & Joint Surg. 8:171 (Jan.) 1926.

knock-knee. The knee should be kept completely extended during the correction of a flexion deformity of the hip. Simple subcutaneous fasciotomy is considered advisable even in mild degrees of deformity in cases in which all three deformities are present, as the time required for complete correction is materially shortened. In children above the age of 6 years, when all three deformities are present a more radical procedure is advised. The iliotibial band should be completely divided and in addition the fascia should be cut laterally as far as the biceps tendon and mesially to the middle of the anterior surface of the thigh.

Traumatic Chondropathy of the Patella.—Traumatic chondropathy is a term that Freund³⁰ applies to a condition of localized osteoarthritis of the patella which he has observed in seven cases. He recognizes three stages of the process. In the first there is a localized elevation of a small portion of the cartilage on the posterior surface of the patella. The surface is intact, but the cartilage feels soft and elastic. In the second stage the cartilage is lacerated in several longitudinal fissures. This is followed by a gradual necrosis of the cartilage until in the third stage the subchondral bone lies bare and is rough and hard. From this stage the process goes on to a general osteoarthritic change of the entire joint. The typical diagnostic sign is the production of pain by pressing the patella against the femur when the knee is flexed, although this sign is absent when the knee is extended. In the latter position the pain may be elicited by moving the patella firmly over the lateral condyle. The treatment consists in excision of the necrotic area. In some cases the opposing surface of the trochlea is likewise affected and must also be excised. Complete recovery was obtained in all cases after operation.

[ED. NOTE.—Some of us have encountered this condition as part of a generalized osteoarthritic involvement of the knee, but we would be cautious in regarding it as an entity or in expecting any marked improvement from operation.]

Calcaneal Spurs.—Lewin³¹ emphasizes the fact that calcaneal spurs are not necessarily of gonorrheal origin. Other organisms, metabolic disturbances, trauma and foot strain may produce similar results. Painful heels and the demonstration of spurs on roentgen-ray examination make the diagnosis clear. The prognosis is stated to be good unless there is an arthritis present. He warns against the removal of the spurs unless this can be done with little operative trauma. The size of the spur has no relation to the amount of trouble it may cause.

[ED. NOTE.—We do not agree with Lewin in regarding the spur as the cause and the painful heel as the effect. We have seen many

30. Freund, H.: *Zentralbl. f. Chir.* 53:707 (March 20) 1926.

31. Lewin, Philip: *Calcaneal Spurs*, *Arch. Surg.* 12:117 (Jan.) 1926

cases in which the spur had undoubtedly been present for years before the symptoms were noted. We regard most of these spurs as osteophytic manifestations of a chronic arthritis similar in every way to the lipping at the margins of joints. The pain is the result of an active inflammatory process, often a bursitis, and with rest and protection will disappear even though the spur persists. Relief following operation in many cases is to be ascribed more to the enforced rest than to the removal of the spur.]

(To be continued)

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SURGERY OF THE LUNG

EXPERIMENTAL LOBECTOMY AND PNEUMECTOMY*

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Our interest in lobectomy and pneumectomy was derived from a desire to remove lobes from dogs in which we had established lung abscesses¹ for the purpose of studying the lesion at various stages of development without killing the animal. In a review of the literature on this particular subject, one certain method was chosen which to us seemed to embody correct surgical principles and to which we have added several refinements in technic. The added danger of an abscessed lung with which we were confronted necessarily submitted the method to an unusually severe test in comparison with the experimental work of others in which normal dogs were used. Nevertheless, our results proved highly satisfactory.

Lobectomy and pneumectomy received their first scientific experimental investigation in 1881 when Gluck² removed one entire lung in six dogs and fourteen rabbits. With the exception of two rabbits all of the animals died in between seven and ten days with pleuritis and pericarditis. The following conclusions were drawn: The operative procedure is well tolerated; the stump lives and forms part of the cicatrix; with careful asepsis healing will take place and no serious results will occur. Marcus³ in 1881 experienced similar results. Independently of Gluck, Schmid⁴ likewise performed experiments in lung surgery. In eight partial apical resections in dogs, there were five deaths

* From the Laboratory of Surgical Research, the Lakeside Hospital and the Western Reserve University School of Medicine.

1. Schlueter, S. A., and Weidlein, I. F.: Postoperative Lung Abscess: An Experimental Study, to be published.

2. Gluck, T.: Experimenteller Beitrag zur Frage der Lungen-exstirpation, Berl. klin. Wchnschr. 18:645, 1881.

3. Marcus, quoted from Murphy, J. B.: Surgery of the Lung, J. A. M. A. 31:151 (July 23); 208 (July 30); 281 (Aug. 6); 341 (Aug. 13) 1898

4. Schmid, H.: Experimentelle Studien über partielle Lungenresektion. Berl. klin. Wchnschr. 18:757, 1881.

and three recoveries. Four of the deaths resulted from suppurative pleuritis and one from acute phenol (carbolic acid) poisoning. Block's⁵ experiments were discouraging. All of the animals operated on, five rabbits and four dogs, died from a septic pleurisy. Even in other experiments in which single lobes were removed from dogs, only two animals recovered. The researches of Biondi⁶ in 1882 were more successful and were the best obtained in these early investigations. Tubercle bacilli were injected into the lung with the hope of producing localized pulmonary tuberculosis. Rabbits, cats and dogs were used. In eleven total extirpations of one lung, four died from a septic pleuritis. The results of Zakharevitch⁷ in 1890 equaled those of Biondi. He experimented on thirteen rabbits and eleven dogs. Two operations on rabbits and three on dogs were fatal. Mass ligation at the root of the lung was done with silk and iodoform was applied to the stump. In 1891 Willard⁸ performed a successful experimental pneumectomy in one dog by suturing the stump, ligated *en masse*, into the wound. The disastrous results experienced by the first investigators were likewise experienced by Murphy⁹ in 1898. In a series of nine dogs in which pneumectomy was performed, there was only one recovery. Eight dogs died soon after the operation, usually from a septic pleuritis.

With the exception of the results obtained by Biondi and Zakharevitch, these early experimental lung resections were successful in only a small percentage of the experiments. They served, however, to show that the removal of a lung by ligating the hilum was possible, and that no dangerous sequelae arose if the element of infection was avoided.

Green¹⁰ resected parts of the lung in fourteen dogs. Seven developed a septic pleuritis. Tiegel¹¹ considered mass ligation a primitive method. In three dogs in which this method was employed, the bronchus reopened after four days, eight days and three weeks, respectively. In other dogs simple ligation of the isolated bronchus resulted in pressure necrosis and a reopening of the lumen after from two to three days.

Because of such poor results Tiegel developed the following technic: A mass ligature of silk was placed about the hilum (catgut is absorbed

5. Block: Experimentelles zur Lungenresektion, Deutsche med. Wchnschr. 7:634, 1881.

6. Biondi, D.: Lungenextirpation bei experimenteller lokalisirter Tuberculose, Wien. med. Jahrb., 1884, p. 207.

7. Zakharevitch, quoted by Willard, DeForest: Experiments in Pneumonectomy and Pneumonotomy, Tr. Coll. Phys. 13:133, 1891.

8. Willard (footnote 7).

9. Murphy (footnote 3).

10. Green, N. W.: The Positive Pressure Method of Artificial Respiration, Surg. Gynec. Obst. 2:512, 1906.

11. Tiegel, M.: Experimentelle Studien über Lungen- und Pleurachirurgie, Mitt. a. d. Grenzgeb. d. Med. u. Chir., supplement 3, 1907, p. 789.

transudate and not infected. Simple ligation of the hilum was all that was done. The results of Schlesinger¹⁷ were similarly poor. One lung was removed from seventeen dogs. Only five lived. The bronchial stump was doubly ligated with silk and covered over with a fold of pericardium. In the opinion of Quinby and Morse¹⁸ the method of Meyer seemed the most accurate and successful. Thirty-eight pneumectomies were performed on dogs with only eight deaths. The difficulty of pushing in a large crushed portion of the main bronchus on the right side was met by treating each of the primary bronchi separately.

In 1914 Henschen¹⁹ suggested the procedure of introducing a roll or plug of fascia into the lumen of the divided bronchus and closing the stump over it. The problem was undertaken experimentally by Giertz,²⁰ but the method was modified somewhat in that the crushed bronchial stump was first sutured with silk mattress sutures and then covered with small fascial transplants sutured with silk to the peribronchial tissues. This was in turn covered with pleura and pericardium. Ten large dogs were operated on. There were no pleural infections and only two fatalities from "Spannungspneumothorax." Kawamura²¹ removed one lung from twenty-three dogs. The method as devised by Tiegel was usually employed, but without the proximal bronchial ligature. He concluded that the method of Willy Meyer was not always possible if the bronchial stump was too short. In only six cases could this method be carried out. There were only two dogs in which death was caused by leakage from the bronchial stump. Similar good results were obtained by Heuer and Dunn.²² Of the twenty-three dogs operated on there were thirteen recoveries and ten deaths. Six deaths were due to distemper and only two of the dogs died from an acute pneumothorax because of an intentionally poor closure of the bronchial stump. All the various methods previously attempted were tried and good results

17. Schlesinger, A.: Experimentelle Untersuchungen über Lungenoperationen unter inter thorakaler Insufflation, *Verhandl. d. deutsch. Gesellsch. f. Chir.* 40 Kong. 2:448, 1911.

18. Quinby, W. C., and Morse, G. W.: *Experimental Pneumectomy: The Application of Data So Obtained to the Surgery of the Human Thorax*, Boston M. & S. J. 165:121, 1911.

19. Henschen, K.: Experimente zur intrathorakalen Lungenchirurgie, *Beitr. z. klin. Chir.* 90:373, 1914.

20. Giertz, K. H.: Ueber Exstirpation von Lungen und Lungenlappen mit Versorgung des Bronchialstumpfes durch frei transplantierte Fascia lata, *Zentralbl. f. Chir.* 41:1433, 1914.

21. Kawamura, K.: Experimentelle Studien ueber die Lungenexstirpation, *Deutsche Ztschr. f. Chir.* 131:189, 1914.

22. Heuer, G. J., and Dunn, G. R.: *Experimental Pneumectomy*, *Bull. Johns Hopkins Hosp.* 31:31 (Feb.) 1920.

tures is the method of choice. The rigid cartilaginous rings continually tend to separate the opposed bronchial walls and if the meager blood supply of the bronchus is interfered with by rough and careless handling of the stump necrosis of the tissues and a reopening of the lumen is sure to follow, thereby establishing a sudden, direct communication between the air passages and the pleural cavity.

The bronchus is composed mainly of cartilaginous tissue, a tissue that is prone to undergo degenerative changes when subjected to slight traumatic injury. A poor blood supply increases the existing tendency of such structures toward degeneration and failure to participate in a reparative process. Even a slight degree of trauma to the vascular structures about the bronchus may, therefore, interfere sufficiently with the blood supply to hinder or prevent healing. In any operation on the bronchus, great care must be taken not to dissect away and destroy too much of the peribronchial tissue for this tissue contains the blood vessels supplying the bronchial wall. The freeing of the bronchus from its enveloping connective tissue seems to have been an important factor in the failures of many investigators.

Briefly, the ideal procedure would seem to be one in which the element of infection could be eliminated, and in which manipulations and traumatisms of the stump are reduced to a minimum. In our opinion successful removal of a lobe or lobes is dependent solely on the technic that will insure an aseptic air-tight closure of a divided bronchus. The invagination method, originally proposed by Meyer, with certain added modifications, we believe, meets such requirements. The method attempts to simulate the technic used in an appendectomy and is as follows:

METHOD

The dog is given a preliminary injection of one-sixth or one-fourth grain (0.01 or 0.016 Gm.) of morphine and anesthetized with ether administered by a cone. After anesthesia is complete, the animal is placed on the right or left side, depending on whether the left or right pleural cavity is to be entered. A rubber tube, slightly smaller in diameter than the inside diameter of the trachea, is then inserted into the trachea and connected to an apparatus²⁵ for interrupted insufflation anesthesia. The thorax is shaved and the skin cleansed with soap, water, alcohol and mercuric chloride (1:3,000 solution). Sterile drapings are placed about the proposed incision and the entire procedure is carried out with a careful aseptic technic. An incision is made through the skin

25. We have used the Erlanger double cylinder apparatus, by means of which air mixed with varying amounts of ether vapor is forced intermittently under slight pressure into the air passages. The air returns from the lungs through the space between the intratracheal tube and the trachea.

over and parallel to the fourth interspace extending from the sternum to the posterior axillary line. The platysma, latissimus dorsi and intercostal muscles are cut, and the parietal pleura is punctured with a blunt instrument. The pleura is incised with scissors and the wound margins are held retracted with a self-retaining retractor. A large enough opening is produced by this incision to permit easy palpation of any lobe of a

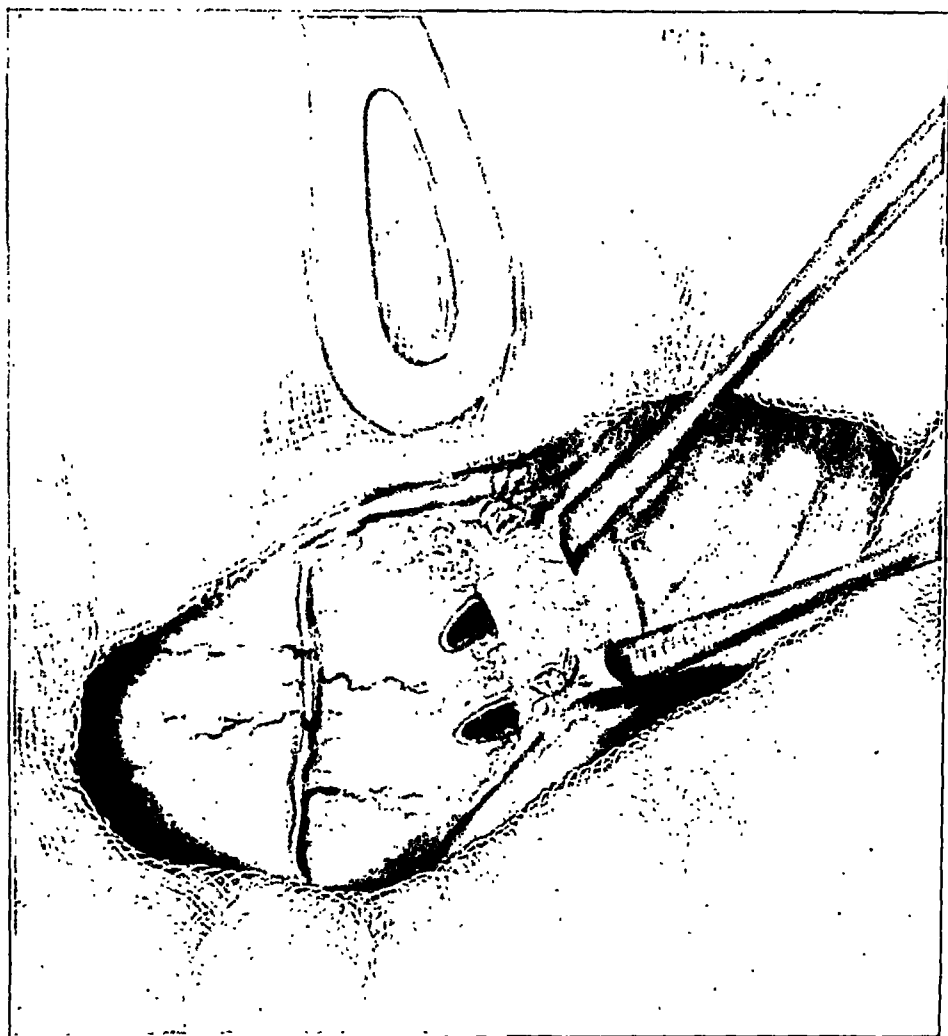


Fig. 1.—The left lower lobe hilum has been exposed; the artery has been divided between a distally placed ligature and two centrally placed ligatures; the bronchus is being isolated.

lung, and the opening in the chest wall is so situated as to allow free access to the hilum. When the pleural cavity is entered, the degree of aeration of the lungs is regulated. Regardless of whether an entire lung or a single lobe is to be removed, the first procedure consists in isolating and ligating the artery. In a pneumectomy, the main branch of the pul-

monary artery is dissected free near the base of the heart. If only the lower lobe is to be removed, the vessel is freed from the vascular sheath lateral and posterior to the bronchus (fig. 1). The artery is isolated; two silk ligatures are placed centrally; one silk ligature is placed peripherally, and the vessel is severed between ligatures. The next step consists in freeing each respective lobe bronchus. Extreme

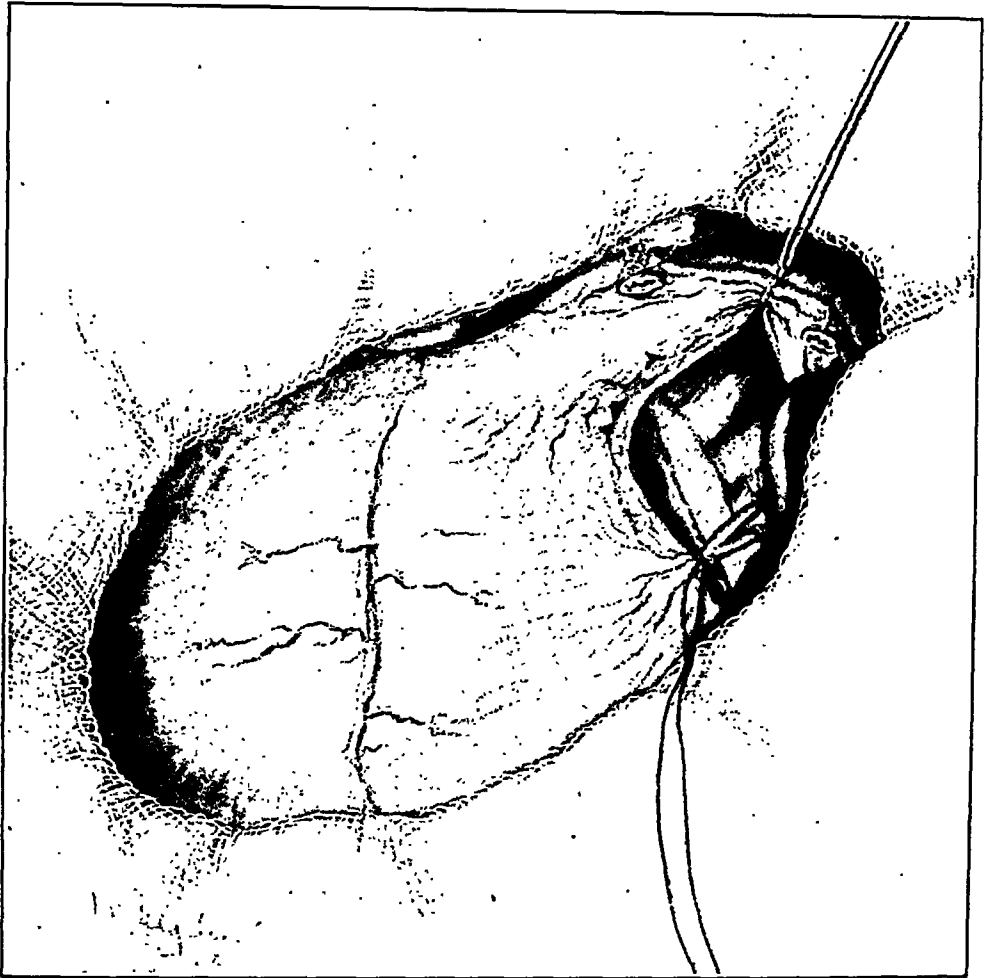


Fig. 2.—The bronchus with attached peribronchial tissues has been ligated distally; the lobe has been pushed laterally to expose the pulmonary veins which are about to be divided between ligatures.

care must be exercised not to strip away too much peribronchial tissue. The structures are carefully dissected away from the point of entrance of the bronchus into the lobe to a centrally situated point that will allow sufficient space for the placement of two ligatures. A plexus of nerve fibers, including the vagus, lies posteriorly and medially in close relationship with the bronchus so that care must be taken not to disturb these structures. While the lung is in a deflated condition, each bronchus is

ligated near the lobe with linen and the ends are left long so that the threads may be used for traction. Further manipulations of the lobe can now be carried out without the danger of spilling accumulated secretions into other parts of the bronchial tree. Likewise, the further progress of the operation is not so much interfered with after the constant refilling of the lobes with air ceases.

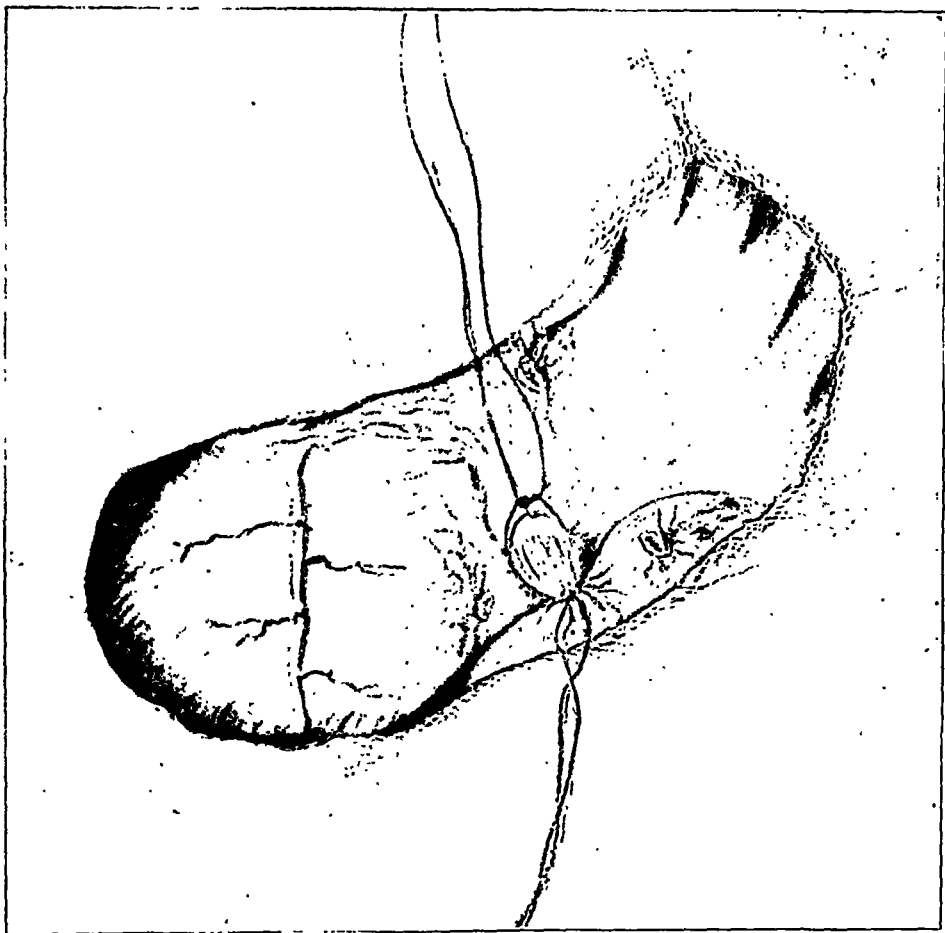


Fig. 3.—The bronchus has been crushed just central to the distal bronchial ligature; a ligature of no. 1 chromic catgut is being placed about the upper portion of the crushed area; the bronchus is then severed between the two ligatures with a knife and both stumps are cauterized with phenol and alcohol.

The lobes are now pushed laterally to bring the pulmonary veins into view (fig. 2). Two or three of these vessels emerge from each lobe and after combining into one or two larger veins pass directly toward the base of the heart. The wall of each vein is exceedingly thin and the vessel may easily be torn across during the dissection. After each vessel is ligated separately at both ends with silk, the veins are cut between the ligatures. The danger of further bleeding having thus been

eliminated, attention is directed toward treating the bronchus. At a point just proximal to the linen ligature the bronchus is crushed with a clamp and a ligature of no. 1 chromic catgut is placed about the upper portion of the crushed area (fig. 3). The ends of this ligature are left long and gauze packs are placed about the bronchus. The bronchus is

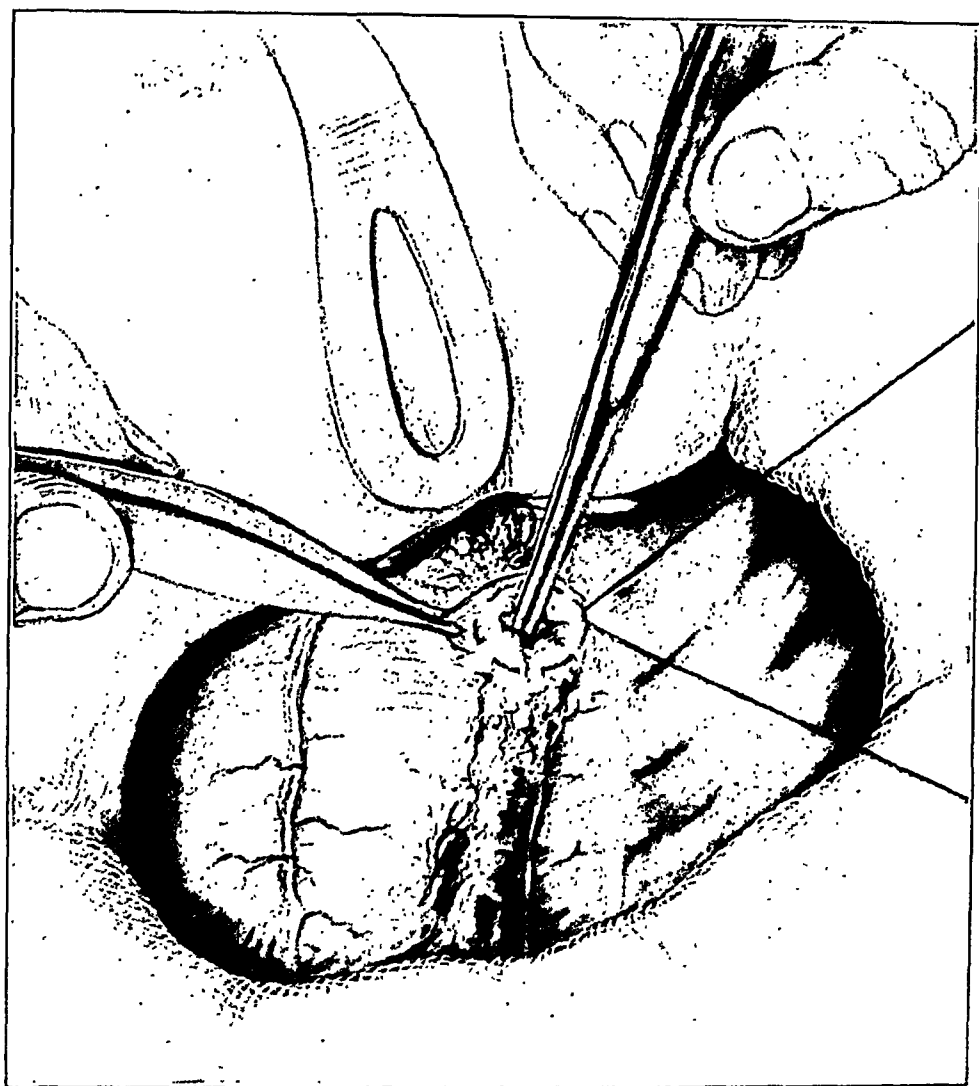


Fig. 4.—The lobe has been removed; a purse string of no. 1 chromic catgut has been placed into the bronchial wall and the stump is being invaginated.

severed with a knife between the two ligatures, the knife is discarded, and both ends of the stump are cauterized with phenol and alcohol. The gauze prevents pleural contamination. The lobe is then removed, and any pleural adhesions present are carefully separated by blunt and sharp dissection. Other lobes are similarly removed. A purse string of no. 1 or zero chromic catgut is then placed in the bronchial wall a short

distance from the stump, care being taken that the actual wall of the bronchus is included in the small needle bites *without perforating* into the lumen of the bronchus. A French needle is best adapted for this purpose. With a tooth forceps the assistant firmly grasps the bronchial

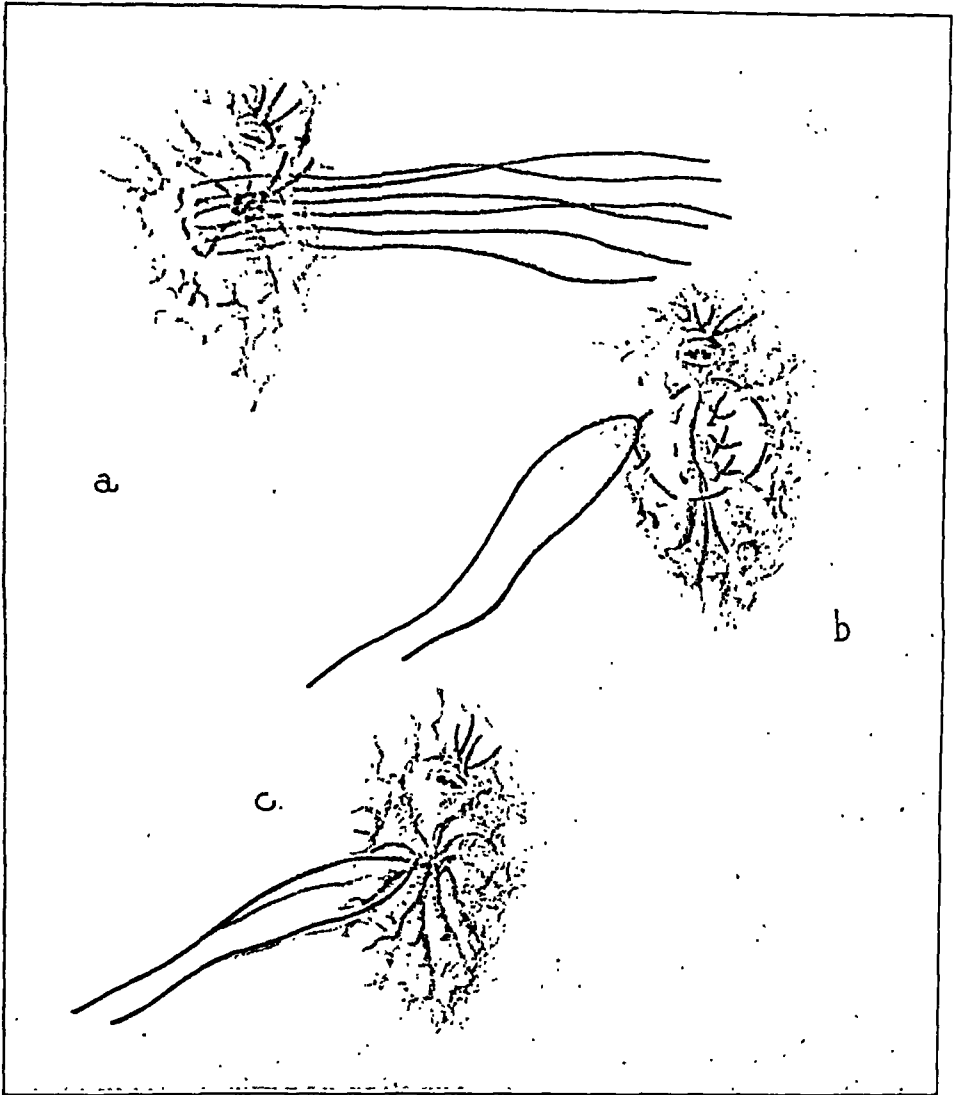


Fig. 5.—(a) Mattress sutures of silk have been placed into the bronchial wall across the stump; (b) the mattress sutures have been tied to reinforce the invagination; a purse string of silk has been placed into the peribronchial tissues; (c) the peribronchial tissue has been pulled over the layer of mattress sutures.

wall above the purse string at a point directly opposite the purse string knot. With these two points held anchored, the assistant invaginates the stump while the operator ties the knot (fig. 4). If the purse string is properly placed and the two fixed points are properly selected, we

believe that there should be no difficulty in invaginating any bronchial stump. We have been able to perform this procedure in every contemplated instance. In the case of a primary bronchus, the stump was easily invaginated. To further reinforce the closure, three mattress sutures of silk are also placed across the stump. These sutures are likewise placed into the bronchial wall but do not penetrate the lumen. A final purse string is placed in the loose peribronchial tissue to cover the layer of mattress sutures (fig. 5).

It is not necessary to attempt suture of the pleura. The opening in the chest wall is closed by merely placing two interrupted sutures of no. 1 chromic catgut about the upper and lower ribs bordering the wound. The sutures can be placed through holes drilled in the ribs as described by Friedrich,²⁶ thereby eliminating the necessity of including the intercostal vessels of the lower rib. The pleural cavity can then be made air-tight by suturing the fascial covering of the ribs and intercostal muscles. Before the pleural cavity is completely sealed, the lungs are inflated to expel as much air as possible. The remainder of the wound is sutured in layers and the skin edges are approximated with a buried subcuticular running stitch of silk. The closed incision is sealed with a collodion gauze dressing to prevent the possibility of a secondary infection. The wound and the entire chest are further protected with a bandage. If careful asepsis is observed, there is no necessity for further dressings. The bandage and collodion dressing are removed after ten days at which time the wound will be perfectly healed.

RESULTS

A single lobe was removed from twenty-four dogs (accompanying table). A septic embolus had been injected intravenously into each of these animals at some time previous to the operation, and in a great many of the experiments a lung abscess was present in the removed lobe. In a few of the animals in which the lesion had existed for a longer period of time, a healed area of fibrosis was demonstrable. Special precautions had to be observed in ligating and tying the bronchus in those operations in which we were dealing with a lobe containing a large abscess. The operative technic as described in the foregoing was not evolved until a series of experiments were performed in which various methods were employed to close the bronchial stump. There were eleven operations in which the following methods were used: (1) a mass ligation of the hilum; (2) a simple ligation of the bronchus; (3) a simple ligation of the bronchus plus a covering of peribronchial tissue, and (4) a suturing of the divided bronchus with silk. The ends of both stumps were always cauterized with phenol and alcohol.

26. Friedrich, P. L.: Die Chirurgie der Lungen, Arch. f. klin. Chir. 82:1147, 1907.

Lobectomies and Pneumectomies: Experimental Data

| Experiment | Lobes Removed | Operative Method* | Duration of Lesion | Lesion in Removed Lobe | Days Lived after Operation | Cause of Death | Condition of Bronchial Stump | Remarks |
|------------|--|--|--------------------|------------------------------------|----------------------------|-------------------------------------|------------------------------|--|
| 1 (Y 11) | Left lower lobe | Mass ligation at hilum; stump not cauterized | 19 days | Area of fibrosis | 23 | Diffuse pulmonary gangrene; empyema | Healed | Wound healed by first intention; source of infection obscure |
| 2 (Y 13) | Left lower lobe | Simple ligation..... | 11 days | Two small abscesses | 1 | Pyopneumothorax | Bronchus open | Ligature had sloughed away |
| 3 (Y 14) | Left lower lobe | Simple ligation..... | 14 days | Area of fibrosis | 87 | Killed | Healed | Killed because of mange |
| 4 (Y 27) | Right lower lobe and right middle lobe | Simple ligation..... | 27 days | Small abscess | Still living | | | |
| 5 (Y 45) | Right lower lobe | Simple ligation..... | 12 hours | Septic embolus in artery | Still living | | | |
| 6 (Y 9) | Left lower lobe | Peribronchial purse string | 14 days | Small abscess | 29 | Bilateral empyema, cause obscure | Healed | Wound healed by first intention; dog perfectly well until a few days before death, except for mange |
| 7 (Y 18) | Left lower lobe | Peribronchial purse string | 10 days | Small abscess | Still living | | | |
| 8 (Y 21) | Left lower lobe | Peribronchial purse string | 33 days | Area of fibrosis | 57 | Diffuse pulmonary gangrene; empyema | Healed | Wound healed by first intention; source of infection obscure |
| 9 (Y 24) | Right lower lobe | Peribronchial purse string | 33 days | Fibrosis of cavity almost complete | Still living | | | |
| 10 (Y 30) | Right lower lobe | Peribronchial purse string | 16 days | Small abscess | 31 | Not determined | Healed | Lungs and pleurae normal |
| 11 (Y 43) | Right lower lobe | Bronchus sutured with silk | 18 hours | Septic embolus in artery | Still living | | | |
| 12 (Y 19) | Left lower lobe | Invagination stump.... | 31 days | Small abscess | Still living | | | |
| 13 (Y 20) | Left lower lobe | Invagination stump.... | 6 days | Large abscess | 63 | Killed | Healed | Killed because of mange |
| 14 (Y 29) | Left lower lobe | Invagination stump.... | 23 days | Small abscess | 23 | Killed | Healed | Killed because of distemper |
| 15 (Y 31) | Left lower lobe | Invagination stump.... | 23 days | Large abscess | 40 | Starvation (?) | Healed | Lungs and pleurae normal |
| 16 (Y 33) | Right lower lobe | Invagination stump.... | 19 days | Area of fibrosis | Still living | | | |
| 17 (Y 36) | Right lower lobe and right middle lobe | Invagination stump.... | 21 days | Large abscess | 13 | Distemper | Healed | Animal had distemper at time of operation; a consolidated right middle lobe also was removed |
| 18 (Y 37) | Right lower lobe | Invagination stump.... | 17 days | Area of fibrosis | Still living | | | |
| 19 (Y 38) | Left lower lobe | Invagination stump.... | 16 days | Small abscess | Still living | | | |
| 20 (Y 39) | Right lower lobe | Invagination stump.... | 12 days | Large abscess | Still living | | | |
| 21 (Y 40) | Right lower lobe | Invagination stump.... | 13 days | Area of fibrosis | 105 | Killed in flight | Healed | Pleural cavities clear; wound clean; marked consolidation of right middle and left upper lobes |
| 22 (Y 41) | Left lower lobe | Invagination stump.... | 8 hours | Septic embolus in artery | 2 | Bronchopneumonia | Securely closed | |
| 23 (Y 42) | Left lower lobe | Invagination stump.... | 4 hours | Septic embolus in artery | Still living | | | |
| 24 (Y 44) | Right lower lobe | Invagination stump.... | 24 hours | Small abscess | 4 | Empyema | Securely closed | Wound slightly infected; pleural infection must have resulted from a slip in the operative technique |
| 25 (Y 50) | Right pneumectomy | Invagination stumps... | 4 days | Abscess in right lower lobe | Still living | | | |
| 26 (Y 53) | Left pneumectomy | Invagination stumps... | | None | Still living | | | |
| 27 (Y 50) | Left pneumectomy | Invagination stumps... | 4 days | Abscess in left lower lobe | 4 | Empyema | Securely closed | Wound infected; pleura grossly infected at time of operation |
| 28 (Y 60) | Right pneumectomy | Invagination stumps... | 4 days | Abscess in right middle lobe | Still living | | | |

* Unless otherwise noted the pulmonary vessels were ligated individually, the bronchus was ligated with no. 1 chromic catgut and sectioned between ligatures. Both stumps were cauterized with phenol and alcohol. A purse string of no. 1 chromic catgut was used in those cases in which the bronchial stump was invaginated. Silk was used for reinforcing mattress sutures and for the peribronchial purse string.

1. In the one experiment in which the hilum was ligated *en masse* with no. 1 chromic catgut, the animal lived for twenty-three days after the operation (experiment 1, dog Y 11). At necropsy a bilateral empyema and gangrenous lesions in the remaining left lung were found. The bronchial stump was healed. The source of the infection was difficult to determine, but the possibility of pleural infection by bacteria of low virulence originating from the stump at the time of the operation had to be considered.

2. In four experiments the bronchus was simply ligated with a ligature of no. 1 chromic catgut. In one animal (experiment 2, Dog Y 13) the bronchus reopened after four days and death resulted from a pyopneumothorax. Two animals (experiment 4, Dog Y 27, and experiment 24, dog Y 45) are still living and one (experiment 3, dog Y 14) was killed after eighty-seven days because of mange. The healed bronchial stump consisted of dense fibrous tissue.

3. In five experiments the ligated stump was covered with peribronchial tissue by using a purse string suture of silk. One animal (experiment 6, dog Y 9) died after twenty-nine days from a bilateral empyema and one (experiment 8, dog Y 21) after fifty-seven days from a bilateral empyema and lung gangrene. Another (experiment 10, dog Y 30) in which the cause of death could not be determined died on the thirty-first postoperative day. At necropsy no lesions of the lungs or pleura could be found. In each of these three dogs the bronchial stump was healed. It was difficult to understand why the signs of fatal pleural infection were not recognized until late in the postoperative period. The dogs seemed to be well until a few days preceding death. In each case the wound in the chest wall had healed by first intention, and, as previously discussed, the infection probably originated from bacteria of low virulence carried to and implanted on the pleura from the stump at the time of the operation. The other two animals (experiment 7, dog Y 18, and experiment 9, dog Y 24) are still living.

4. In the fourth method the severed bronchus was closed with a continuous suture of silk. The postoperative course was uneventful and the dog is still living (experiment 11, dog Y 43).

In the thirteen remaining experiments the bronchial stump was treated by the invagination method and in none of these animals did sloughing or reopening of the stump occur. Only two deaths were attributed to the operative procedure. In experiment 22, dog Y 41, death occurred on the second day following operation. At necropsy a marked consolidation of the right middle and upper lobes was found, but the pleural cavities were free from infection. Death probably resulted from a bronchopneumonia. A bilateral empyema was responsible for the second death (experiment 24, dog Y 44). The wound in the chest wall was grossly infected. The bronchial stump was securely

closed so that the pleural infection probably resulted from a break in the aseptic technic. One animal (experiment 15, dog Y 31) died forty days after operation but the cause of death was not determined. At necropsy marked emaciation was the only observation. Distemper was the cause of the death in experiment 17, dog Y 36. At the time of the production of the lung abscess the animal already had some signs of distemper, viz., cough, apathy, anorexia and a slight purulent discharge from the nostrils. At operation twenty-one days later, the right lower lobe contained a large abscess and the right middle lobe was completely consolidated. It was decided to give the operative technic a critical test, and the consolidated lobe was likewise removed. The animal was quite ill during the first few days following the operation; the nasal discharge was quite profuse and at times quite hemorrhagic. For a time, however, the general condition seemed improved, but the animal failed to overcome the infection and death occurred on the thirteenth postoperative day. At necropsy the remaining lobes of the lung showed the typical distemper conditions. Both pleural cavities, however, were free from infection and the bronchial stumps as well as the external chest wound were perfectly healed. This would seem to illustrate how the pleural cavity can be entered with perfect safety even in the presence of severe pulmonary infections if rigid aseptic technic is adhered to. The foregoing case illustrates also how entire lobes can be removed if the bronchus is recognized as being infected and is dealt with accordingly. With the exception of one animal, which was killed in a fight, the remaining animals are still living.

The following typical protocol illustrates the invagination method:

PROTOCOL

EXPERIMENT 17.—Dog Y 36, weighing 13.2 Kg., Nov. 23, 1925, was given one-fourth grain (0.016 Gm.) of morphine. Thirteen days previously a septic embolus had been freed into the jugular vein. Subsequent roentgenograms had shown a developing abscess in the right lower lobe. On the day preceding lobectomy, the right middle lobe was seen to show consolidation (fig. 6). The dog had had distemper for some time, and it was thought that the consolidated right middle lobe was a part of the disease. Under ether intratracheal insufflation the animal was anesthetized and the right pleural cavity was entered through the fourth intercostal space. Examination revealed no adhesions about the lower lobe. The middle lobe was solid and reddish with numerous white areas presenting on the surface of the lobe. The lower lobe was first removed. The pulmonary artery to the lobe was isolated, ligated and sectioned between ties. The bronchus was then isolated and ligated distally with linen. The veins were ligated distally and centrally and severed between ligatures. The bronchus was then crushed with a clamp just central to the linen ligature. A ligature of no. 1 chromic catgut was placed about the crushed area, the bronchus was cut across between the ligatures with a knife, and both stumps were cauterized with phenol and alcohol. A purse string of no. 1 chromic catgut was placed in the wall of the bronchus, and the stump was invaginated. The stump was further reinforced with three mattress

sutures of silk and a peribronchial purse string gave additional covering. The right middle lobe was similarly treated. The pleural cavity was closed with two pericostal sutures of no. 1 chromic catgut, and the wound was closed in layers with a running stitch of silk. A buried subcuticular stitch approximated the skin. The lower lobe showed a large abscess (fig. 7), and the middle lobe showed a diffuse bronchopneumonia.

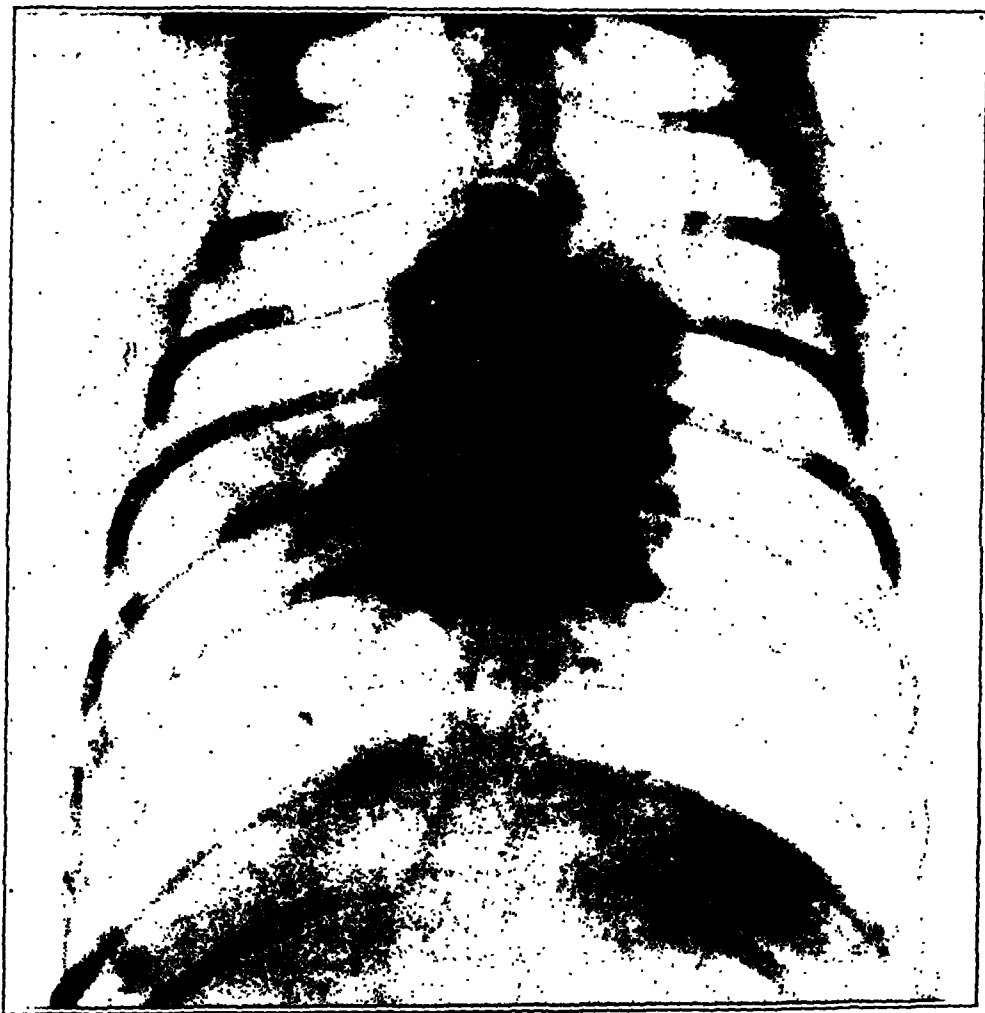


Fig. 6.—Dog Y 36, experiment 17, nineteen days after an infected embolus had been released into the jugular vein; the bit of lead contained in the embolus indicates the position of the thin walled abscess cavity in the right lower lobe; the area of density in the region of the right middle lobe shows the degree of lung consolidation, the result of a complicating distemper. The right middle and lower lobes were removed the following day.

November 25, the dog appeared quite ill. A purulent, hemorrhagic discharge exuded from the nostrils. There was an occasional cough.

November 30, the dog appeared to be improving steadily. The nasal discharge was less in amount, the cough was less severe, and more food was eaten. The external wound had healed by first intention.

December 6, the animal was found dead in his cage. The symptoms had gradually become more pronounced. At necropsy a hemorrhagic, purulent exudate was present throughout the bronchial tree. There was a small amount of clear hemorrhagic fluid in both pleural cavities. There were no pleural adhesions. The bronchial stumps were well healed. The remaining lobes of the lung had the characteristic distemper appearance.

In four dogs one entire lung was removed according to the invagination method by treating each respective lobe bronchus separately. Three



Fig. 7.—The right lower lobe of Dog Y 36, experiment 17, removed at operation; a section taken through the specimen shows the contained abscess cavity.

dogs (experiment 25, dog Y 50; experiment 26, dog Y 53, and experiment 28, dog Y 60) are still living. Dog Y 50 had an abscess in the right lower lobe. The lung removed from dog Y 53 contained no lesion. Dog Y 60 had an abscess in the right middle lobe. One dog (experiment 27, dog Y 59) in which the left lung was removed died on the fourth postoperative day. The lower lobe contained a large abscess and many pleural adhesions were present at the time of the operation. The pleural membranes were markedly inflamed, and it was thought that the dog would probably not survive the operation. We were forced to close the pleural cavity because of the inadvisability of

external drainage which in a dog would certainly produce a fatal pneumothorax. We were not surprised, therefore, to find a well developed empyema at necropsy. The bronchial stump had remained closed. In this particular experiment invagination of the left primary bronchus was done.

CONCLUSIONS

It is evident that direct comparisons cannot be drawn between these experimental results and the results obtained by other investigators. The majority of the lobes removed in the foregoing experiments contained abscesses in various stages of development, and the possible danger of pleural infection following operation was therefore greatly increased. Realization of this handicap necessitated extreme care in the removal of such a lobe and because of the many failures others have experienced in removing one lobe or an entire lung in which our added complication was not present, we felt somewhat dubious about the final outcome. In the first experiments, therefore, we were content in removing only the abscessed lobe. However, our results with lobectomy were encouraging, and the successful removal of a lobe containing an abscess we attribute to the avoidance of infection from the bronchial lumen. A method was devised which would recognize and eliminate this possible source of infection and which would simulate as nearly as possible the technic employed in an appendix operation. This method, we believe, can be applied to any sized bronchus, although we cannot submit sufficient experimental proof. Invagination of a primary bronchus was, however, easily accomplished in one pneumectomy experiment. Moreover, our experiences have led us to feel that it is not necessary to attempt closure of a primary bronchus in the dog. The risk that an inadequate closure of this structure entails need not be taken. Each bronchus to a lobe can be treated separately as was done in three of the pneumectomy experiments.

Our results also substantiate the work of others that an entire lung can easily be removed from dogs, that the animals survive the operation, that they remain free of any deleterious sequelae, and that the severed bronchus heals by scar tissue formation providing infection has not been introduced.

Clinically, the removal of a lobe of a lung would seem to be a less hazardous procedure if infection from the bronchial lumen were avoided. The method devised in this experimental work may be of some assistance in securing an aseptic air-tight closure of a bronchus in clinical cases.

ABSCESSSES AND INFLAMMATORY TUMORS IN THE SPINAL EPIDURAL SPACE (SO-CALLED PACHYMENINGITIS EXTERNA) *

WALTER E. DANDY, M.D.

BALTIMORE

Two recent cases of inflammatory tumors in the spinal epidural space presented a picture then unknown to us from a series of spinal cord tumors. In one of the cases the lesion, a tubercle, developed so rapidly as to suggest an extradural abscess; the other, of several months' duration, was looked on as a tumor, despite the high cell count, until the presumed level of the growth was carefully marked out preparatory to operation. When the predicted level of the tumor was found to be identical with an old scar over the spine of a dorsal vertebra, the diagnosis of some inflammatory lesion affecting the cord, though of ill-defined character, appeared to be a probability. When the history had been taken, the patient expressed the belief that his trouble dated from a severe carbuncle of which this directing scar was the result. About the same time my associate, Dr. Frank Ford, recalled an almost identical case, an inflammatory extradural mass, the symptoms of which followed closely on a carbuncle of the back and continued to increase long after its healing. Curiously, these three inflammatory tumors were situated at almost the same cord level and all were confined to the dorsal side of the spinal canal. These facts seemed to suggest not isolated and bizarre spinal infections but rather examples of a well defined type and doubtless also dependent on an anatomic background.

A search of the literature revealed not only a few additional inflammatory extradural masses but also a greater number of acute purulent infections in the epidural space. Strangely enough most, but not all, of these were confined to the same thoracic level and in each the infection was restricted to the dorsal half of the epidural space. There was, moreover, another fact that defined these primary infections as of a special type; namely, similar extradural infections apparently do not develop in the cranial chamber. These infections, therefore, whether acute or chronic, seemed to occur (1) only in the *spinal* epidural space, (2) only in the dorsal half of the spinal canal, and (3) principally in the thoracic region.

An explanation of these findings was sought in the anatomy of the spinal epidural space. However, the current textbooks of anatomy were of little assistance for in none did the epidural space receive more than

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brief mention. Dissection of a cadaver shows that the spinal extradural space is present only dorsal to the spinal nerve attachments. Ventral to the nerves the dura is everywhere closely applied to the bones of the vertebrae and their ligaments from the first cervical to the second sacral vertebra. Below the second sacral bony segment the epidural space surrounds the dura on all sides. The epidural space is filled with fat and loose areolar tissue containing numerous veins.

Of greatest importance are the variations in the size of the epidural space. In the cervical region the space is only potential, there being only a few strands of fibrous tissue and almost no fat between the laminae and dura. The epidural space really begins to appear at the seventh cervical vertebra and gradually deepens along the thoracic vertebrae, attaining a depth of about 0.5 to 0.75 cm. between the fourth and eighth dorsal vertebrae. The space tapers again and becomes shallow between the eleventh thoracic and second lumbar vertebrae. Over the remaining lumbar and the first and second sacral vertebrae the epidural space attains its greatest depth. At the second sacral vertebra the dural envelop ends and a continuation of the epidural tissue fills the caudal end of the sacral canal. Only at the lower terminus of the spinal dura does the extradural space extend ventrally; here for a short distance the dura is encircled by the epidural fat and areolar tissue. The size and shape of the epidural space, therefore, appear to be secondary to the variations in size of the spinal cord. Absent over the cervical enlargement and nearly so over the lumbar swelling the epidural space becomes deepest where the spinal cord or the mass of its roots is smallest, i. e., in the upper dorsal and lower lumbar sections. And the space exists only on the dorsal aspect of the dura.

The spinal epidural space is therefore filled with tissues—fat and loose areolar—which offer a foothold for current hematogenous infections, and the intraspinal location of these tissues makes trauma an important inciting agent in the development of hematogenous infections.

Whether the epidural fat performed any normal function other than serving as a padding can hardly be answered unequivocally. It is easy to believe that it acts as a buffer to trauma but such a protective function would appear to be particularly called for in the cervical region, and here the fat is absent. Nevertheless, it would seem to serve some buffer function to direct traumatic insults in the rigid thoracic region. Under certain pathologic conditions the epidural fat is of no little diagnostic and therapeutic value. Practically all spinal cord tumors cause this bed of fat to be absorbed by continuous pressure; in this way the pressure of the tumor on the cord is withheld for a time to a degree commensurate with the volume of the fatty tissue that is destroyed.

During operations for spinal cord tumors the presence or absence of epidural fat, in the thoracic and lumbar but not in the cervical canal.

is carefully noted and considered a sign of great value. If fat is present a tumor beneath the dura is unlikely though not impossible, whereas the absence of fat indicates pressure absorption and, therefore, an underlying neoplasm. The recent work of Peters¹ should be mentioned in this connection. He has shown a frequent involvement of the epidural tissues from primary infections of the spinal meninges. We have, however, found no other reports of persisting epidural infections after cures in any form of meningitis.

We are not concerned in this article with the most common extensions of tuberculous infections from the bodies of the vertebrae into the spinal canal. Such infections are easily recognized by the characteristic picture of vertebral destruction in association with the evidences of spinal compression. Moreover, the epidural space is involved in these cases only because it lies in the path of further extension of the tuberculous process and not because of any peculiar characteristic of the space or its contents. Furthermore, in paraplegia associated with Pott's disease surgery is contraindicated; at least up to this time the results obtained by laminectomy have not been helpful and have usually done harm.

Nor shall we consider here those remarkable chronic inflammatory hypertrophies of the cervical region described by Charcot and Joffroy as pachymeningitis cervicalis hypertrophica, nor the more extensive dural hypertrophies, involving the entire length of the spinal dura, described by Mills and Spiller.² These proliferations of fibrous tissue, gradually increasing the bulk of the dura on its inner side, grow into and slowly strangle the spinal cord, causing symptoms that are said to resemble syringomyelia. These rare diffuse increments probably arise from the dura; their origin is considered to be syphilitic. Weinberg³ has only recently described a localized mass of fibrous tissue arising from the inner side of the dura and compressing the cord. Although he makes a probable diagnosis of tuberculosis from the histologic picture of giant cells, the Wassermann reaction in the spinal fluid was positive. It would, therefore, appear justifiable to question whether the lesion might not have been a gumma, the more common primary dural affection.

ACUTE INFECTIONS IN THE EPIDURAL SPACE (I)

Abscesses of the epidural space arise in two ways: (1) by direct extension of a contiguous infection, and (2) by metastasis through the blood stream.

1. Peters, R.: Ueber die Entzündung der Extraduralen Gewebes des Rückenmarks bei der Genickstarre, *Deutsche med. Wchnschr.* **32**:1151, 1906.

2. Mills, C. K., and Spiller, W. G.: Case of External Pachymeningitis, Implicating the Entire Ventral Surface of the Spinal Dura, *Brain* **25**:318, 1902.

3. Weinberg, M. H.: Spinal Cord Tumors; Six Cases Including Tuberculosis of Dura, *J. Nerv. & Ment. Dis.* **63**:23 (Jan.) 1926.

Albers, 1833, from Germany has been credited with first reporting an acute infection of the epidural space. Ducheck, 1853, gave to this condition the name peripachymeningitis, which was later changed to pachymeningitis externa. Cases have been reported under both titles. As will be shown later, both appellations are misnomers for the infections are not of the meninges as was then supposed but of the tissues of the epidural space.

In three cases, of Lewitzky,¹⁰ Spencer,¹¹ and Hinz,¹² necropsy revealed no other infection in the body; the abscesses were therefore assumed to be primary in the epidural space. Although Hinz assumed the infection to have probably arisen from a puerperal thrombosis, the extrathecal infection appeared four weeks after a normal pregnancy, the first symptom of the fatal illness being uterine bleeding; no evidence of uterine infection was found at necropsy. Trauma appears to have been an inciting agent in the case of Kaminski and, according to Cassirer, in cases reported by Runge and Pulvirenti.

A study of the accompanying table of acute epidural infections discloses several striking facts. There have been only two recoveries in the entire series of twenty-five cases (Pulvirenti, Taylor and Kennedy⁵): both of these followed drainage of the infection. Apparently in only the four cases subjected to operation was a diagnosis even suspected before the necropsy findings, and except in Taylor and Kennedy's case there is no evidence to indicate that the nature of the lesion was more than roughly guessed. Without exception the acute infections have been fulminating, death usually resulting in two or three weeks; the minimum duration of life is six days and the maximum thirty days.

How effective operative treatment will be for abscesses of this character can, of course, only be conjectured. Much will necessarily depend on the virulence of the organism, the resistance of the patient and the extent of the infection in the epidural space. Tightly sealed within the vertebral canal, an abscess can hardly rupture into the soft tissues and be spontaneously cured. The only possible avenue of escape would be through an operative defect in the laminae.

At first glance it might appear that the structure of the epidural space would preclude any practical operative drainage. From the high cervical region to the sacral canal the epidural space is continuous, i. e., it is not intercepted by mechanical barriers. But relatively poor as fatty tissue is known to be in combating infections, it is actually able to build a barrier of inflammatory tissue and restrict the acute infection to a small fraction of the epidural space. It is not improbable, in fact it seems more reasonable to believe, that the resistance to infections in the epidural space is largely due to the vascular areolar tissue and not to the fat. In only two (Kaminski, Spencer¹¹) of ten cases in which the location of the abscess has been mentioned has the infection spread

10. Lewitzky, P.: Ein Fall von Peripachymeningitis spinalis, Berl. klin. Wchnschr. 14:227, 1877.

11. Spencer, N. H.: Case of Idiopathic Inflammation of the Spinal Dura Mater, Lancet, June 14, 1879, p. 836.

12. Hinz, R.: Ueber einen Fall von Perimeningitis purulenta, Deutsche med. Wchnschr. 47:1229 (Oct. 13) 1921.

I. Acute Infections (Abscesses)

| Reported by | Age and Sex* | Secondary to | Primary Origin | Incited by Trauma | Location of Infection | Symptoms of Onset | Pain; Location | Character of Pain | Paraplegia | Paralysis: Time of Onset; Time Until Complete | Bladder or Rectum |
|--|--------------|----------------------------|----------------|-------------------|-----------------------------------|--------------------------|---|-------------------------------------|-----------------------------|---|-------------------|
| Oppenheim ⁶ 1910 | 40 ♀ | Phlebitis (staphylococcus) | Metastatic | .. | VI dorsal to I lumbar | Sudden pain | + Lower thoracic vertebrae and legs | Increasing until terrific | + | 6th day; rapid increase | |
| Hinz ¹² 1921 | 29 ♀ | | Primary (?) | .. | IV to VIII dorsal | Backache | + Back | Backache | + Flaccid | 4th day; sudden | Retention |
| Morowitz ⁴ 1919 | 15 ♀ | Healed furunculosis of leg | Metastatic | .. | Lower thoracic | Sudden terrific pain | + Inguinal region bilateral | Spread next day to back and abdomen | + | 9th day; 1 day | |
| Morowitz ⁴ 1919 | 26 ♂ | | Metastatic | .. | Lower thoracic | Sudden severe pain | + Back and legs | Severe, continuous | None | None; none | |
| Morowitz ⁴ 1919 | 15 ♀ | | Metastatic | .. | | Dizziness and chill | + | Headache | .. | | |
| Cassirer ⁷ 1923 | .. | Furuncle | Metastatic | .. | | | | | + | | |
| Spencer ¹¹ 1879 | .. | | Primary | + | Whole canal | | | | .. | | |
| Lewitzky ¹⁰ 1877 | .. | | | .. | | | | | .. | | |
| Lemoine and Lannois ¹⁹ 1882 | .. | | | .. | | | | | .. | | |
| Mollère ²⁰ 1897 | .. | | | .. | | | | | .. | | |
| Hoestermann ⁸ ... 1913 | .. | Furuncle of neck | Metastatic | .. | V to VII dorsal | | | | .. | | |
| Kaminiski..... 1917 | 15 ♀ | Furunculosis of leg | Metastatic | .. | Whole length | Sudden pain | + Knees; then inguinal and finally in back | Terrific | + Below dorsal II | 9th day; sudden | Retention |
| Link ⁹ 1909 | 40 ♂ | Bronchitis (diplococcus) | Metastatic | No | Lower cervical and upper thoracic | Sudden pain in both arms | + Both arms, shoulder and upper vertebrae | Very severe | + Weakness of arms later | 9th day; sudden | Retention |
| Traube, 1863, cited by Kaminiski | .. | | Metastatic | .. | | | | | .. | | |
| Albers, 1833, cited by Kaminiski | .. | | Metastatic | .. | | | | | .. | | |
| Pulvirenti, 1921, cited by Cassirer | .. | | Primary | + | III-IV lumbar | | | | .. | | |
| Runge, 1920, cited by Cassirer | .. | | Primary | + | | | | | .. | | |
| I. A. Acute Infections (Abscesses), Resulting from | | | | | | | | | | | |
| Taylor and Kennedy ⁵ 1923 | 15 ♀ | Abscess along ribs | | .. | Lower thoracic and lumbar | Pain and chills | + Lower ribs | Severe and sharp | Complete | 13th day; 2 days | Retention |
| Mannkopf, 1864, cited by Kaminiski | .. | Ludwig's angina | | .. | | | | | .. | | |
| Barth, cited by Kaminiski | .. | Puncture wound | | .. | | | | | .. | | |
| Hasse, cited by Kaminiski | .. | Decubitis | | .. | | | | | .. | | |
| Hasse..... | .. | Decubitis | | .. | | | | | .. | | |
| Hasse..... | .. | Decubitis | | .. | | | | | .. | | |
| Dueck, 1853 cited by Kaminiski | .. | Decubitis | | .. | | | | | .. | | |

* In this table ♂ indicates male. ♀ female.

19. Lemoine, G., and Lannois, M.: *Périmeningitis Spinalis Aigue*, Rev. de méd. 2: 533, 1882.

20. Mollère, H.: Note sur un cas de Périmeningite spinale primitive Suppurée, Lyon méd., 1897, p. 143.

Primary or Metastatic

the Direct Extension of Contiguous Infections

[illegible]

| Reported by | Age and Sex* | Secondary to | Primary Origin | Infect- ed by Trauma | Location of Infection | Symptoms of Onset | Pain; Location | Character of Pain | II. Inflammatory Tumors | | |
|---|-------------------|--|-----------------------------|----------------------|---------------------------|-----------------------------|--------------------------|----------------------|---|--------------------|-------------------------------------|
| | | | | | | | | | Paralysis: Time of Onset; Time Until Complete | Bladder or Rectum | Paraplegia |
| Stroubell ¹³ 1898 | 56 ♀ | | Syphilis (?) | .. | III to VI dorsal | Paraplegia and anesthesia | | | Complete | Sudden | |
| Schultze ¹⁴ 1903 | 24 ♂ | | Chronic inflammatory tissue | .. | V to VII dorsal | Pain | + Lower ribs and back | Sudden, excruciating | Partial, spastic | 3 months; 6 months | Disturbed function but no retention |
| Fischer ²¹ 1902 | 41 ♂ | | Syphilis (?) | .. | III to VI dorsal | Pain in vertebrae and legs | + | | + | | Retention and incontinence |
| Mendel ¹⁷ 1900 | .. | | Chronic inflammatory tissue | .. | V to IX dorsal | Pain in head, neck and back | + Head, neck and back | Severe | Partial | 2½ years; partial | |
| Pelz ²² 1917 | 67 ♂ | | Tuberculosis | .. | Middle and lower thoracic | Pain in back | + Back and later legs | | Total | 1½ months | Incontinence (last 2 weeks) |
| Gampers..... 1920 | .. | | Tuberculosis | .. | Lumbar | | | | .. | | |
| Lewis and Buesse ⁹ 1915 | 21 ♀ | | | No | V and VI dorsal | Numbness and pain in legs | Toes | Cramp | Complete | 3 weeks | Slight incontinence in voiding |
| Dandy..... 1926 | 42 ♂ | Direct extension from furuncle on back | Chronic inflammatory tissue | No | V to VIII dorsal | Pain | + Back and sides | Severe, sharp | Partial | 10 months; partial | Incontinence |
| Dandy..... 1926 (Dr. Ford's case) | Middle age ♂ | Direct extension from furuncle on back | Chronic inflammatory tissue | No | V to VIII dorsal | Pain | + Back and waist | Severe, sharp | Partial | 3 months; partial | Incontinence |
| Dandy..... 1926 | 27 ♀ (colored) | | Tuberculosis | + | III to VI dorsal | Pain | + Back and sides | Very severe | Complete | 8 months; 3 days | Incontinence, etc., thereafter |

* In this table ♂ indicates male, ♀ female.

21. Fischer: Ein Fall von Pachymeningitis chronica externa spinalis, Verhandl. d. Gesellsch. deutsch. Naturf. u. Ärzte, 2: 16, 1902.

22. Pelz, A.: Kasuistische Beiträge zur Lehre von den Rückenmarks-Geschwülsten, Arch. f. Psychiat. 58: 175, 1917.

Direct Extension of Contiguous Infections—Continued

(No Abscess)—Continued

| Sensation | Spine: Rigidity; Tenderness | Kernig Sign | Headache | Leukocytes | Temperature | Reflexes | Spinal Fluid | Duration of Life | Operation | Result | Clinical Diagnosis | Remarks |
|---------------------------------------|-----------------------------|-------------|----------|------------|-------------|-------------------------------------|--------------------------|------------------|----------------------|----------------|-----------------------------------|---|
| Absent | | .. | .. | | | Absent | | | | Dead; necropsy | | Reflexes absent; no clonus; granulation tissue tumor, not like tuberculosis—probably syphilis |
| Sensory level gradually became higher | None: V to VI dorsal | .. | .. | | | Increased ankle clonus | | 10 mos. | + | Dead; necropsy | | After 5 weeks the pain improved but quickly became worse when numbness of feet ensued; persisted 7 months, then again disappeared but returned for an hour every time he bent over; pain worse on coughing and sneezing; ankle clonus; died of meningitis after operation; tumor dorsal side of dura; grayish red solid mass 12 cm. long, 1 cm. thick; connective tissue strands and cluster of cells |
| Absent | | .. | .. | | | Increased clonus | | 1 yr. | No | Dead; necropsy | | Mass of fibrinous tissue containing giant cells; thinks it histologically more like syphilis; no evidence of tuberculosis |
| Partial loss | | .. | .. | | | | | 3 yrs. | + | Dead; necropsy | | Tumor 9.6 cm. long; granulation tissue without specific character; no necrosis or giant cells |
| | | .. | .. | | | | | 10 mos. | No | Dead; necropsy | | Pain in legs developed only after 4 months; weakness came soon after; tumor 1 cm. long, 1 cm. thick; all on outer side of dura; granulation tissue with many giant cells and tubercles |
| | | .. | .. | | | | | | | Dead; necropsy | | No involvement of vertebrae |
| Absent | Very little | .. | .. | | | | Normal | Well | Spinal decompression | Well | Tuberculous involvement of cord | Patient was in seventh month of pregnancy when symptoms began; was allowed to go to term and labor was successfully completed; 3 weeks later decompressive laminectomy; indurated mass of fat in epidural space (dura not opened); quick return of function; complete restoration of motor power in 3 years |
| Sensory level | +; + | + | No | | No | Greatly increased Babinski reflex + | 53 cells; xantho-chromia | Well | + | Well | Inflammatory tumor | Pain in back and sides persisted 6 months; since then somewhat diminished; convulsions in legs 1 month; diagnosis of an inflammatory tumor was made before operation; return of function |
| Sensory level | +; + | .. | .. | | No | Greatly increased Babinski reflex + | 9 cells; lymphocytes | Well | + | Well | Tumor | This case is presented by permission of Dr. Ford; the operation was performed in Bellevue Hospital, New York; a firm fibrous mass 6 cm. long and 1 cm. thick removed; return of function |
| Total absence below sensory level | +; + | .. | .. | | | | 15 cells; lymphocytes | Well | + | Well | Tuberculosis of spine and abscess | Struck back 8 months before; pain had persisted since in that spot; any movement intensified pain; return of function; Wassermann reaction from blood and spinal fluid negative; no tubercles seen |

throughout the length of the epidural space. In such instances operative efforts would necessarily be fruitless. In those cases in which the infection has been walled off, there is every reason to believe drainage would result in a cure.

Doubtless operative results will always be dependent on the stage at which the diagnosis is made. It would appear probable that an abscess though at first walled off must, when increasing rapidly and becoming tense, break its plastic barriers and spread up and down the epidural space. An early diagnosis followed by operation may well prevent diffusion and facilitate restriction of the infection. It is fortunate at least that the epidural space and its infections are located on the dorsal side of the spinal dura. Were the abscesses situated ventrally drainage would be extremely difficult if not impossible.

There should be little if any difficulty in arriving at a diagnosis of an epidural abscess when the signs of spinal cord compression (accompanied by fever and leukocytosis) develop and the level of the spinal cord injury is contiguous to a preexisting infection. Nor would it appear that the diagnosis of hematogenous abscesses of the epidural space would offer insuperable obstacles. In fact the signs and symptoms of this group (I) seem to be sufficient distinctly to suggest a clinical entity. In practically all of these cases the symptoms of onset is a terrific, almost unbearable and unrelenting pain (1) in the back, or (2) along the course of the spinal nerves (bilateral), or (3) in the legs. In a previous article these types of pain have been attributed, when caused by spinal cord tumors, to involvement of (1) the vertebrae, (2) the spinal nerves, and (3) the sensory paths in the spinal cord. But these pains are much more severe and persistent in inflammations than when due solely to pressure from a tumor. The pain in spinal tumors, or in fact in any other proved lesion, though seemingly of the same kind, cannot approach in severity or persistence the pains of infection of the epidural space.

The next most impressive evidence of abscesses of the epidural space is the latent period of a few days (from four to nine) between the time of onset of the excruciating pain and motor, sensory and sphincter paralysis. In every instance paraplegia, as well as sensory and sphincter loss, has either been sudden or has become complete within forty-eight hours after its onset. In nearly all cases there has been a sharp bilateral sensory level which may or may not have ascended, doubtless depending on whether the epidural abscess has extended upward or has remained localized. In addition to this characteristic story there is always high fever, tachycardia, leukocytosis (18,000 in three cases) and probably always tenderness and rigidity of the spine. Although there are few records of examinations of the spinal fluid (in two cases organisms were grown in cultures of the cerebrospinal fluid, possibly because the

needle passed through the epidural infection) there must always be an increased cell count (polymorphonuclear cells) as the reaction to an adjacent acute infection. Manometric tests have also not been made in these cases but since the paralyses are evidence of spinal cord compression, a complete block of the spinal canal must surely exist. Such a block was demonstrated in both of our inflammatory tumor cases, in one of which the symptoms of spinal cord involvement developed almost as suddenly as in any of the acute abscesses. Whether an acute epidural abscess may eventually be diagnosed before implication of the spinal cord and before the appearance of a spinal block remains to be seen. At least a pain that appears so distinctive should put us on guard for the earliest sensory or motor changes. Experience has taught us that the more rapidly spinal compression causes paraplegia the more slowly recovery takes place after its relief. Gradual compression of the spinal cord allows a remarkable adjustment to the tumor's bulk; often the spinal cord may be reduced to half its cross sectional volume with little or no loss of function, but after the removal of a slowly growing tumor the recovery of function is very rapid.

The sudden onset of paraplegia in these cases has led to the diagnosis of myelitis or even of thrombosis or embolism. All these conditions should be eliminated by the excruciating pain which for several days precedes paralysis, by the tenderness and rigidity of the spine and by the demonstration of a spinal subarachnoid block. Although meningitis might appear possible because of rigid neck, a positive Kernig's sign, fever and leukocytosis, the sensory and motor level and the cerebrospinal fluid examination, together with the absence of a spinal subarachnoid block, should easily exclude this diagnosis. The possibility of an abscess of the spinal cord might also be considered but the interval of pain that precedes paraplegia in epidural abscesses would doubtless be absent.

INFLAMMATORY EPIDURAL TUMORS (II)

The story in this group of cases is very different. While the pain is of the same general character and extremely severe, it lacks the very sharp onset; it is less fulminating and is prolonged over a period of weeks or months instead of days. The latent period preceding paralysis is far longer and the paralysis is usually slow in developing and usually incomplete. In brief all manifestations are chronic instead of acute. In only two cases (Stroubell,¹³ Dandy¹⁴) did the symptoms of spinal cord compression appear suddenly, and only in these instances and a case

13. Stroubell: Ueber Syphilis der Rückenmarkshäute, Neurol. Centralbl., 1898, p. 1120.

14. Dandy, W. E.: The Diagnosis and Localization of Spinal Cord Tumors, Ann. Surg. 81:223 (Jan.) 1925.

of Lewis and Bassoe¹⁵ was the paraplegia complete. In the remaining cases the motor, sensory and sphincter changes developed so slowly (from three months to two and one-half years) as to suggest tumors rather than infections. Four of these tumors have been described as syphilitic or tuberculous because of the histologic demonstration of giant cells and occasional tubercles. Since the histologic differential diagnosis between syphilis and tuberculosis is so often impossible, it is not safe to assume that all of these cases are due either to syphilis or tuberculosis. In our patient syphilis was excluded by the negative Wassermann reaction in both the blood and the spinal fluid. Tuberculosis seemed more probable because of her race (colored), but tubercles could not be definitely demonstrated in sections of the tumor nor was there any other evidence of tuberculosis in the body. She has, moreover, remained well and free of any symptoms or signs of tuberculosis since the operation, over two years ago. In her case trauma seemed to play a definite inciting rôle; at least she refused to yield from her original story that a pain developed immediately after a blow on the spine and that it persisted in the same spot. And precisely at that spot the tumor was found at operation. A remarkable feature of this case is that an inflammatory tumor probably existed eight months (its gross appearance also supports the slow growth of the tumor) before any symptoms of paralysis and then paraplegia became complete in three days, and without abscess formation.

Four cases of this group would appear to be of staphylococcus origin, those of Schultze,¹⁶ Mendel¹⁷ and Dandy¹⁴ (two). In our two cases the organisms were identified by cultures. In the cases of Schultze and Mendel the infections were probably of metastatic origin. In our two cases the epidural infections were undoubtedly due to the direct extension of the outskirts of deep middorsal carbuncles. These two cases strikingly demonstrate how differently infections are handled by different tissues. In both of our cases the original carbuncle in the soft tissues of the back had long since healed (five and thirteen months) leaving only a scar, whereas at the end of this time the areolar and fatty tissues of the epidural space were still struggling to wall off the same organisms, which could not be destroyed. In slowly subduing these infections the newly formed inflammatory tissues assumed the proportions of tumors. That living organisms were still present in the connective tissue masses was demonstrated by bacterial stains of the sections,

15. Lewis, Dean; and Bassoe, P.: *Frazier's Surgery of the Spine and Spinal Cord*, 1918, p. 922; *Surg. Gynec. Obst.* 20:489, 1915.

16. Schultze, F.: *Zur Diagnostik und Operativen Behandlung der Rückenmarks hautgeschwülste*, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* 12:153, 1903.

17. Mendel, K.: *Meningo myelitis unter der Bilde eines Rückenmarkstumors*, *Berl. klin. Wchnschr.* 46:2239, 1909.

by the presence of minute abscesses in the connective tissue and in one case by the growth of *Staphylococcus aureus* from cultures of the tumor at operation. Moreover, in both these cases the infection was again lighted up by the trauma incident to the operation; the wounds promptly broke down and from one wound *Staphylococcus aureus* was grown in culture.

In all these chronic inflammatory tumors (except in Lewis' case) pain in the back, though far less excruciating than in the epidural abscesses, has been much more severe than from neoplasms whether of intradural or extradural origin. The cell count from the cerebrospinal fluid in our three cases was 9 (tubercle), 15 and 53—all lymphocytes.

The age of the patients afflicted with inflammatory tumors averages higher than of those with abscesses. The series of cases is, however, too limited to warrant conclusions on this point. It is also worthy of note that with one exception¹⁸ these inflammatory tumors have been in the thoracic epidural space and nearly all between the third and ninth vertebrae. Again the series is too small to allow us to consider this too significant. Two facts, however, are suggested as a possible explanation of this greater incidence in the thoracic region: (1) carbuncles and furuncles are more common in the thoracic than the lumbar region; (2) spinous processes are more superficial in the thoracic region and therefore the spine is protected by less soft tissues and is also more susceptible to trauma.

All the tumors have been well formed and firm. In one of our cases it was of cartilaginous consistency and so tightly bound to the dura that considerable force and sharp dissection with a periosteal elevator was necessary to strip it from the dura. The masses of inflammatory tissue averaged about 1 cm. in depth; the longest was 12 cm. One of ours weighed 15 Gm.

In our three cases the tumor was removed. An equally good result, however, was obtained by Lewis¹⁵ by a simple decompression laminectomy. It is interesting that in his patient operation was delayed over two months to allow the completion of a full term pregnancy. It is also worthy of note that pain was not a conspicuous feature in the case—the sole exception—through the involvement of the fat with inflammatory tissue seemed similar to the other cases in this group.

REPORT OF THREE CASES OF CHRONIC INFLAMMATORY TUMORS OF THE EPIDURAL SPACE

CASE 1.—A large, well nourished man, aged 42, was referred by Dr. L. F. Barker because of gradually progressive paraplegia and anesthesia, suggestive of a spinal cord tumor. The patient persisted in dating his illness from a carbuncle and a series of boils in the back thirteen months before. During

18. Gampers, E.: Beitrag zur Pathologie und Therapie der Erkrankungen der Cauda Equina, Jahrb. f. Psychiat. u. Neurol., 1920, p. 40.

this illness he suffered severe pains in the back and sides and after healing of the infection the character and the intensity of these pains persisted. For the following six months the pains steadily increased; all efforts to allay them were futile. Since then the pains in the sides has been present only at times but the terrible backache had remained practically unchanged.

Three months previously numbness appeared almost synchronously in both legs. Two weeks later the patient's gait became affected and it was soon necessary to use a cane in walking. Loss of equilibrium and of motor power progressed gradually. One month later both legs became spastic and involuntary jerkings (he aptly termed them "convulsions") appeared. The spastic contractions became so powerful that it was often impossible voluntarily to counteract the muscular pull. At times the legs would be fixed in the extended position and again strongly flexed at the hips and knees. The contractions were very painful. The numbness seemed gradually to extend up the legs and abdomen and finally settled at a level above the umbilicus. Girdle pains and a feeling of constriction developed and persisted in this region. Sneezing produced a queer tingling in his feet.

On admission he was able to walk a few yards with great effort and only when supported, but as attempts at walking brought on the painful clonic contractions he was reluctant to stand. All motor and sensory functions in the upper extremities were normal.

Dr. Barker's examination showed in addition to the motor loss a sharp girdle of hyperesthesia at the eighth thoracic segment with marked loss of sensation to pain, touch and temperature below this level; almost complete loss of muscle sense in both feet; greatly exaggerated knee kicks and Achilles reflexes; a bilateral positive Babinski reflex and ankle clonus. The epigastric reflexes were obtainable but the abdominal and cremasteric reflexes were absent. There had been no incontinence of urine or feces. Examination of the spinal fluid showed xanthochromia, heavy globulin and fifty-three lymphocytes.

It was Dr. Barker's opinion, in which I concurred, that the patient's condition was due to a spinal cord tumor, the localization of which was quite accurately determined by the sharp girdle of altered sensation. We were disturbed by the high cell count and heavy globulin, neither of which could be satisfactorily explained.

Despite the patient's persistence in associating his symptoms with the series of boils on his back thirteen months before, there seemed to us little possibility of lesion from this source at this late date. However, when according to custom the presumed site of the tumor was scratched by a scalpel for operative localization the marker bisected a round scar over the sixth thoracic spine, obviously the scar of an old carbuncle. The association of the scar and the marker for orientation was too striking to disregard as a coincidence. At once it seemed that there must be some relationship between the old inflammatory process and his tumor. Accordingly I dropped out of the operation to convey this impression to Dr. Barker but both of us felt that the lesion was such as to require exploration.

At operation when the laminae of the sixth and seventh vertebrae were removed a reddish brown mass at once appeared in lieu of the normal extradural fat. The tumor was so fibrous and lacking in cellular elements that an extradural sarcoma, the only likely form of tumor in this location, appeared inconceivable. It was thought to be an inflammatory mass. Frozen sections verified this diagnosis. To get above and below this growth it was necessary to remove extra laminae, the fifth and eighth, i. e., the laminae of four vertebrae in all.

Epidural fat was then encountered both above and below the tumor mass and dissection was begun from below upward. The mass was so tightly bound to the dura and it so overhung the lateral margins of the dura that dissection in toto made no progress. The tumor was then bisected longitudinally in the midline, which was the deepest part of the mass; it presented on cross section a semilunar shape. Even then blunt dissection of the tumor was impossible. So tightly was the tumor bound to the dura and so hard was the tumor that I believe the spinal dura could have been pulled from its attachment before the mass would have separated or the tumor broken. With a sharp periosteal elevator the mass was cut away from the dura, there being scarcely a suggestion of a line of cleavage. The inflammatory mass after removal measured 11 cm. long, 2 cm. deep, and was as wide as the spinal dura which



Rigid mass of inflammatory tumor removed from the epidural space in case 1; microscopically the tumor was purely inflammatory.

it covered; it weighed 15 Gm. Minute foci of cellular tissue were seen throughout a cut section of the tumor, also little islands of infiltrated fat. There was no evidence of pus. Under the microscope the cellular foci were seen to be miliary subacute abscesses, polymorphonuclear cells predominating. They were surrounded by dense walls of fibrous tissue. Unfortunately cultures of the tissues were not made at operation.

The entire wound quickly broke down from infection. *Staphylococcus aureus* was grown from cultures of the wound, the organisms doubtless liberated from the miliary abscesses of the tumor and stimulated to renewed activity by the operative trauma.

Two months after operation the patient was discharged with the wound healed. Recovery of function, though slow, has been gradual and complete. Two and a half years later he remains perfectly well.

The tumor, therefore, is of inflammatory character. It surely arose from direct extension of the infection of an old carbuncle of the back (thirteen months before operation) into the extradural fat.

CASE 2.—The second patient was a colored woman, aged 27. She was admitted to the medical service of the Johns Hopkins Hospital because of a rapidly progressive paraplegia. Eight months before she fell down three or four steps, striking her back in the upper thoracic region. She spent the day in bed because of pain in her back and side. The pain in the back had persisted without remission, but the pain in the side had disappeared at times, though the longest free interval has not been greater than a week. The pain in the back was dull and aching; that in the chest, sharp and cutting. She had not been able to bend forward, even to look down, because any movement of the back intensified the backache. For the last three weeks the pains in the back and chest had been particularly severe; they "cut off her wind" if she bent her body.

Nine days before operation both legs suddenly gave way so that she could scarcely walk. A loss of sensation developed synchronously and rapidly extended upward until a sharp level was reached at the lower costal margin on both sides. She volunteered that she had since been unable to contract her abdominal muscles.

Seven days before admission she developed incontinence and three days later incontinence gave way to retention, catheterization being necessary. There had never been spasticity.

Examination showed total flaccid paralysis of both legs; the upper extremities were unimpaired. A sharp sensory level crossed the thorax just below the xiphoid process; below this line there was complete anesthesia to pain, touch and temperature; there was total loss of muscle sense. The epigastric and abdominal reflexes were absent. The left knee kick was feebly present but the right knee kick and both ankle jerks were absent. There was no response to plantar stimulation. Marked tenderness was elicited on deep pressure about the spine of the fourth, fifth and sixth thoracic vertebrae. The spinal fluid examination made on the medical service showed fifteen cells, all leukocytes.

In Queckenstedt's test the cerebrospinal fluid rose 20 mm. from a base level of 115 mm. following compression of both jugular veins; but the level was not restored on release of the jugular pressure. Several times this was repeated with the same results. Roentgen-ray examination of the spine was negative; the Wassermann reaction from the blood and spinal fluid were negative.

Air injection into the spinal canal showed a sharply defined block in the spinal canal at the fourth thoracic vertebra. Immediately on the introduction of the air into the spinal canal her original pain was duplicated and intensified. The injected air did not reach the cranial chamber.

Because of the great rapidity of the paralysis a tuberculous abscess was suspected, probably in relation to a diseased vertebra, though roentgen-ray examination was negative.

At operation a mass of inflammatory tissue was removed from the extradural space between the third and fifth thoracic vertebrae, inclusive. The mass was firm and sharply defined above, below and laterally. It covered only the dorsal aspect of the spinal dura from which it was completely removed.

Microscopic sections showed chronic inflammatory tissue containing many giant cells. The pathologic diagnosis was tuberculous granuloma.

Return of motor and sensory functions began two weeks after the operation and progressed slowly. She could walk in three months. It is now two years since the operation and the patient has remained perfectly well. Her gait is absolutely normal.

CASE 3.—To the foregoing cases I append a third by permission of my associate, Dr. Frank R. Ford. The patient was an Italian laborer who was under Dr. Ford's care at Bellevue Hospital, New York. He had been admitted because of weakness and stiffness of the legs. Five months before his entry into the hospital he was infected with a series of furuncles over the back. These caused severe pain over the back and around the waist. For several weeks after the furuncles had healed, the pain continued severe and the spine was so tender that he could not lie on his back. Three months after the furuncles had healed, the patient noticed weakness and stiffness in his legs. This progressed slowly and a month later he had to give up work.

The patient was a fairly robust man of middle age. Several scars of old boils were seen over the back; one of these was directly over the spinous process of the seventh thoracic vertebra. Though very spastic he could walk without support with difficulty. Cutaneous sensibility was partially lost below a well defined level crossing just above the umbilicus. Sense of position and vibratory sense were greatly diminished. Bladder control was beginning to be affected. All the tendon reflexes were increased in the legs; there was a bilateral positive Babinski reflex; no abdominal reflexes were obtainable. The spinal fluid was clear and colorless, and there were nine cells per cubic millimeter, all lymphocytes.

At operation a firm fibrous mass was removed from the posterior surface of the dura beneath the laminae of the fifth, sixth, seventh and eighth thoracic vertebrae. The mass was about 1 cm. thick and about 6 cm. long. It did not extend under the anterior surface of the dura. The tumor was recognized to be of inflammatory origin. Cultures were taken and *Staphylococcus aureus* grew therefrom. The wound broke down and healed by granulation. A year later the patient walked almost normally. This case is practically a twin to case 1.

SUMMARY AND CONCLUSIONS

1. In three cases of extradural inflammatory tumors, around which a group of acute and chronic cases have been assembled from the literature, the infections arise either from direct extension of contiguous infections of the soft parts or from hematogenous metastasis of an infection in remote parts of the body.

2. We believe the symptoms of these infections to be sufficiently characteristic to represent a clinical syndrome.

3. The spinal epidural space with its content of fat and areolar tissue determines the presence and location of these infections. This space has no prototype in the cranial chamber; it is situated almost entirely on the dorsal half of the spinal dura; its size varies inversely with that of the spinal cord and cauda equina.

4. Although all the acute infections have run a fulminating and fatal course, except two that were drained, it is hoped that with an early and accurate diagnosis, operative treatment (drainage) may be effectual in saving both life and function.

5. The chronic inflammatory tumors of the epidural space are perhaps more difficult of differential diagnosis than ordinary tumors. It should, however, usually be possible. Their treatment is surgical removal as with any other tumor. The dura should not be opened because of the danger of a renewed infection.

strangulation of the abdominal contents was noted. The abdominal respiratory movements were normal and there was no tenderness, rigidity or muscle spasm.

The preoperative impression was that the patient had an umbilical hernia which would be reducible, possibly a Meckel's diverticulum with partial intestinal obstruction.

Operation.—Dr. Cullen operated, March 30. Abdominal exploration was easily performed, no abnormalities being noted except for the cecum. Here on its antero-lateral aspect, including the lateral half of the anterior taenia coli, was seen a round defect sufficiently large to admit the tip of the index finger for about 2 cm. On palpation a small mass could be felt through the wall of the cecum

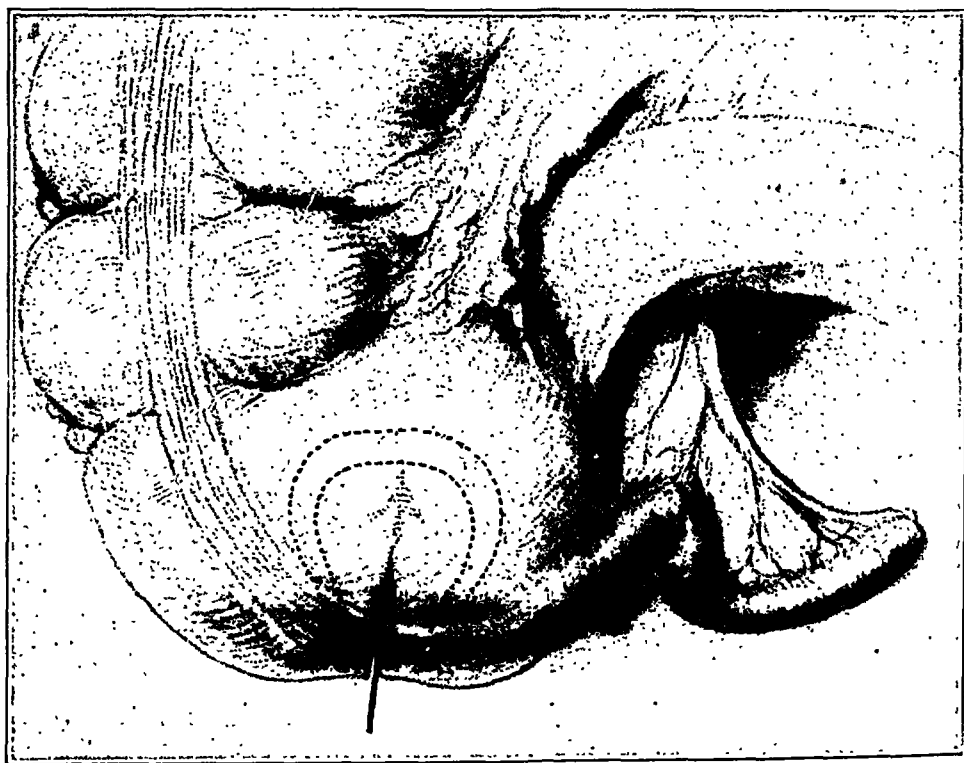


Fig. 1.—Situation of cecal invagination in relation to appendix and anterior taenia coli.

apparently attached to the intestinal wall at the point where the defect, just mentioned, existed.

Figures 1 and 2 represent in a semidiagrammatic manner the condition found at operation. Pressing on the anterior and medial aspect of the cecum caused the mass to vanish, and simultaneously an invagination to unfold, bringing to view the serous aspect of the invaginated portion which appeared hyperemic, somewhat roughened, and possibly slightly puckered. On palpation this area felt of cartilaginous consistency. One lymph gland at the anterior-superior aspect of the ileocecal junction was definitely enlarged, elastic and smooth. The neighboring mesenteric glands showed no macroscopic change. The ileum and cecum elsewhere appeared normal while the appendix showed some dilatation of its subserous vessels.

The pathologic area in the cecum was excised, a flexible curved Kocher intestinal forceps being applied so as to prevent the intestinal contents from soiling the operative field. The defect was closed with two rows of No. 2 plain catgut, the appendix was removed and the abdominal wall closed in layers, one small drain of protective material being left in situ and removed after twenty-four hours.

The patient's convalescence was uneventful. She left the hospital on the eighth day following the operation and is now living and well after three years, no recurrence of symptoms having been noted.

Pathologic Examination.—The gross specimen consisted of a small piece of tissue, somewhat irregular in outline, measuring 2.5 by 3 cm. and from 4 to 6 mm. in thickness. On one surface (serosa) the tissue was pale gray, smooth

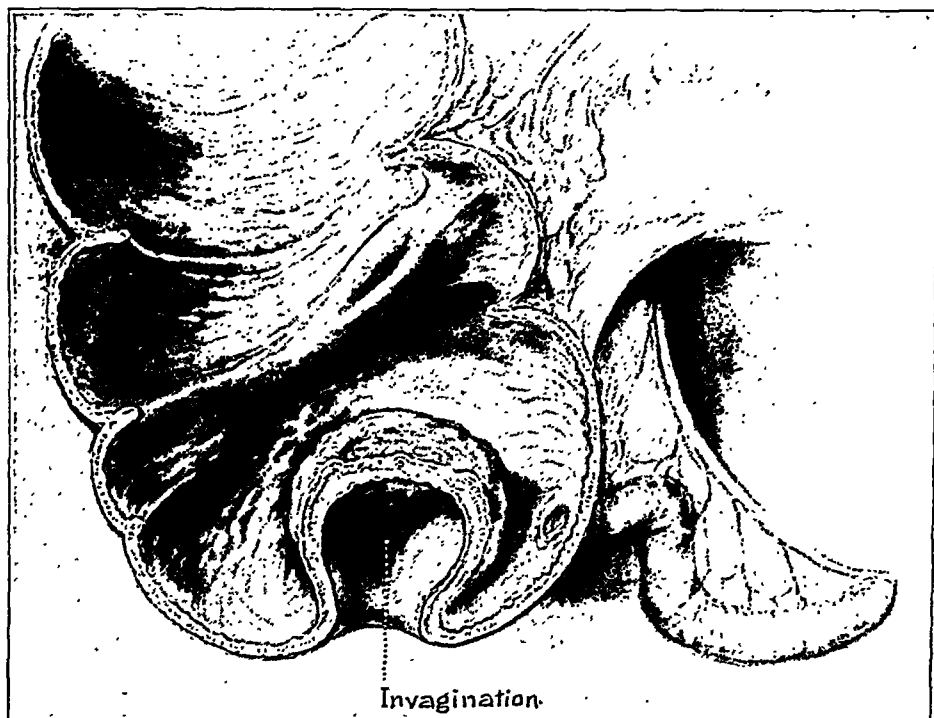


Fig. 2.—Schematic drawing of cecum in coronal section showing relation of invaginated portion to orifice of vermiform appendix and ileocecal valve.

and glistening. On the other surface (mucosa) there was an elevated central area, about 12 mm. in diameter, which was purplish red, opaque and dull in appearance and on palpation was rather firm in consistency. No exudate was seen. On section the cut surfaces were smooth and dark purple for a depth of from 2 to 3 mm.; beyond this point the tissue in its remaining thickness was pale gray and glistening. The area just described was surrounded by a narrow zone of pale gray, glistening and delicate mucosa, which was about normally movable on its underlying structures.

Microscopic sections were made of tissue fixed in Zenker-formaldehyde solution and stained with hematoxylin and eosin. Sections from the less abnormal areas at the periphery of the specimen showed the large intestine, the epithelium of which appeared essentially normal except for one area where a thin layer

of overlying exudate (just to the left of *X* in figure 3) was seen. Beneath this exudate the superficial mucosa cells showed definite impairment in staining reaction. There was moderate extravasation of red blood cells into the interglandular stroma of the mucosa; some large round wandering cells were present, and here also hyaline thrombi situated in the capillaries were not infrequent. The submucosa showed considerable edema and in its superficial portion a considerable infiltration with polymorphonuclear eosinophils and erythrocytes. The tunica muscularis was quite distinct and apparently unchanged except that it (both circular and longitudinal layers) together with the subserosa showed a characteristic appearance of edema. The serosa was intact.

As one approaches the area beneath *X* in figure 3 one notes a gradual intensification of the process described above. At *X* an abrupt transition occurs marked by hemorrhage in the submucosa and complete obliteration of the architecture of the mucosa, muscularis mucosae and the superficial half of the submucosa, these now being represented by a pink staining, reticular mass. In the most superficial portion of this necrotic process no cellular elements are



Fig. 3.—Microsection of intestine ($\times 9.6$) showing, to left of *X*, some edema and only a moderate degree of cellular infiltration, the latter being limited to the mucosa and submucosa and at *X* an abrupt change, which, at the extreme right of the section, involves the entire thickness of the intestine in a necrotic process; the right margin of this section represents the midpoint of the necrotic zone and corresponds to the midpoint of the apex of the invagination in figure 2.

seen. Beneath this acellular zone a zone of dense round cell infiltration occurs, a few polymorphonuclear leukocytes are also present, and an occasional capillary containing a fibrinous thrombus is seen. The fibers of the tunica muscularis, both circular and longitudinal, show marked impairment in staining reaction and indistinctness in outline. There is little if any cellular infiltration here or in the subserosa which, however, shows evidence of marked edema.

Sections stained for connective tissue by both Mallory's and van Gieson's methods showed no increase in fibrous stroma.

Sections stained for bacteria by a combination of Goodpasture's and Weigert's stains as described by MacCallum¹ showed here and there a super-

1. MacCallum, W. G.: A Stain for Influenza Bacilli in Tissues, *J. A. M. A.* 72:193 (Jan. 18) 1919.

ficial area in the necrotic tissue in which some gram-positive cocci and large, broad bacilli and many small gram-negative bacilli were seen. The deeper portions of the necrotic zone and the remaining thickness of the intestinal wall contained no demonstrable bacteria and no protozoa were seen.

The groups of ganglion cells lying between the layers of the tunica muscularis and those occurring in the submucosa, in the less abnormal portions of the intestinal wall, possessed normally staining elements. Their nuclei contained the usual well defined and markedly chromophilic nucleoli and there was a well defined nuclear membrane surrounded by an ill defined cytoplasm which took a faint eosin stain. As one approached the more pathologic portion of the intestine one was impressed by the ability of these neurologic elements to retain their morphology, though their staining properties were somewhat impaired, while the surrounding muscle fibers showed distinct loss of outline and lessened staining reaction. In those portions of the sections showing the most advanced pathologic change neurologic elements could no longer be identified.

The pathologic lesion described in the foregoing is explainable, we believe, leaving out of consideration for the present the mechanism of the invagination, as the result primarily of a purely mechanical process, namely, the interference with the circulation to the invaginated portion of the cecum, with its consequent series of tissue changes resulting successively in edema, necrosis and thrombus formation, peripheral cellular infiltration and extravasation and, finally, in *superficial* invasion of the necrotic mucosa by bacteria of the intestine. In short, the process partakes of the nature of an infarction.

Particular attention is invited to the fact that the most advanced pathologic changes are present at the apex of the invagination and that the central portion of the apex shows the most extensive change of all in that the entire thickness of the intestine shows evidence of degeneration, lessening in degree, however, from within outward. The remainder of the invaginated intestine, from the apex peripherally, shows a corresponding decrease in edema and cellular infiltration.

The frequency of occurrence of a pure cecal type of intussusception is difficult to estimate from a most extensive review of the literature owing to the fact that by far the greater number of reports represent pure clinical observations, in which histologic examinations form the exception rather than the rule and accurate detailed descriptions of the operative findings are not recorded. For example, Rushmore,² in a review of 237 cases, reports only two instances of a cecal type of intussusception. On the other hand, Hipsley,³ in a study of forty cases in which the origin of the intussusception was noted, reports nineteen in which the process began at the tip of the cecum "just above the junc-

2. Rushmore, J. D.: Intussusception, *Ann. Surg.* 46:210-223, 1907.

3. Hipsley, P. L.: A Résumé of Fifty-One Cases of Intussusception, *M. J. Australia* 2:383-386 (Nov. 9) 1918.

tion of the anterior and lateral taenia coli." Likewise Clubbe,⁴ referring to the place of origin of invaginations, in a most careful study of his findings in 100 consecutive operations for intussusception in children, notes that in the ileocecal variety of intussusception the starting point is in the caput caeci and not at the valve, as is generally assumed to be the case. This free end of the cecum is often a little difficult to unfold, after the reduction of the main part of the intussusception, remaining as a "small cup-shaped depression with hard walls." Clubbe in his remarks on intussusceptions beginning in the ileum notes also that the first infolding seems to start at the side of the bowel and always opposite the mesenteric attachment.

Joyce⁵ reports in detail a case of advanced intussusception which on reduction showed "the end of the cecum inverted, thick and hard," forming on palpation a "button-like structure," it being necessary to "knead" the cecum to restore it to its proper shape. Thomas⁶ reports a case probably less advanced than any of those preceding. This occurred in a boy of 13; the end of the cecum was invaginated, having carried in with it that portion to which the appendix was attached. The walls of the cecum were much thickened owing to edema, but the ileocecal valve was not involved. Possibly the earliest instance encountered is one reported by Shacklock.⁷ From his description it probably resembles more closely than any of the others the case that forms the motif for this paper. Shacklock's patient was a boy, aged 7 years, in whom the cecum just lateral to the vermiform appendix had invaginated the remainder of the cecum in an upward direction for about 1 inch (2.5 cm.). In the foregoing reports, unfortunately, no pathologic descriptions are given other than those observed at operation.

Shacklock's case is the only one encountered in the literature which in its apparent incipency resembles closely the case reported in this article, and it is particularly regrettable that no histologic study was available; however, manipulation was sufficient in this case to reduce the invagination, appendectomy was performed and the patient made an uneventful recovery.

A case reported by Cole⁸ is given here in considerable detail, because the tumor that he describes as accompanying the intussusception most closely resembles the microscopic appearance of the diseased section

4. Clubbe, C. P. B.: One Hundred Consecutive Laparotomies for Intussusception in Children, *Brit. M. J.* 1:1327, 1905.

5. Joyce, C.: An Unusual Form of Intussusception, *M. J. Australia* 2:540, 1914.

6. Thomas, T. T.: Intussusception of Head of Cecum Without Involvement of Ileocecal Valve, *Tr. Philadelphia Acad. Surg.*, 1918-1919, 21:110, 1920.

7. Shacklock, G. A. S.: Three Cases of Intussusception, *Guy's Hosp. Gaz.* 31:36, 1917.

8. Cole, A. F.: A Case of Intussusception (Cecocolic) and Remarks on the Pathology of the Accompanying Tumor, *China M. J.* 22:13-16, 1908.

found in our case, though the intussusception was well advanced in Cole's case and could, therefore, hardly be considered incipient.

Cole's case is one of cecal intussusception, about 8 inches (20.3 cm.) of the cecum and ascending colon being found within the more distally situated ascending colon. Reduction was easily performed, the cecum and appendix coming into view when reduction had been completed. Near the base of the appendix the walls of the cecum were puckered, hard and thick. This area, with the appendix, was excised and a tumor mass presented, projecting about one-half inch (1.27 cm.) into the intestine. The mass was greenish black in appearance, smooth and about seven-eighths inches (2.1 cm.) in diameter. Microscopically, "it was seen to consist in the main of widely dilated spaces filled with leukocytes, red cells, and in places with a colloid material perhaps of lymphatic origin. There is marked round celled inflammatory infiltration at the margin of the growth." . . . "The surface of the tumor is smooth and the ordinary glandular nature of the cecal mucosa is replaced by a homogeneous mass of disintegrating cells with different staining properties from the deeper portion. Here and there a suggestion of the original tubular nature can be seen. . . . The muscularis mucosae is somewhat atrophic but there is no evidence of malignant invasion."

Cole considers the inflammatory process in his case as primarily mechanical in etiology due to some constricting process, and ventures the suggestion of a reverse peristalsis causing this portion of the cecum to become engaged in the orifice of the ileocecal valve.

It would appear that Cole's case is altogether similar to the one reported in this article and that the inflammatory tumor he describes probably had its origin in an identical manner.

Cases described as invagination of the cecum due to inflammation at the base of the appendix such as reported by Rogers,⁹ Wright and Knowles,¹⁰ together with another group of cases described by Struthers,¹¹ Brown,¹² Connor,¹³ Monsorrat,¹⁴ Rolleston,¹⁵ Waterhouse¹⁶ and others

9. Rogers, J. T.: Invagination of the Bowel Due to Inflammation at the Base of the Appendix, *St. Paul M. J.* **11**:458-463, 1909.

10. Wright, G. A., and Knowles, R.: Chronic Intussusception of the Appendix into the Cecum: Operation; Recovery, *Brit. M. J.* **1**:1470, 1897.

11. Struthers, J. W.: A Case of Chronic Intussusception with Complete Inversion of the Vermiform Appendix, *Lancet* **2**:1345, 1906.

12. Brown, W.: A Case of Intussusception of the Vermiform Appendix, *Scot. M. & S. J.* **12**:333-335, 1903.

13. Connor, F. P.: Intussusception of the Vermiform Appendix, *Lancet* **2**:600, 1903.

14. Monsorrat, Keith: Intussusception of the Vermiform Appendix, *Liverpool M.-Chir. J.* **21**:68-78, 1901.

15. Rolleston, H. D.: Prolapse of the Mucous Membrane of the Appendix into the Cecum, *Edinburgh M. J.* **4**:21-26, 1898.

16. Waterhouse, H. F.: Intussusception of the Vermiform Appendix, *Brit. M. J.* **2**:1505, 1897.

as intussusceptions of the vermiform appendix, are interesting and may properly be mentioned here, for they are mere variations in situation and extent of the same process and our case is probably illustrative of them all as they appeared in their incipency.

Masson and Leriche¹⁷ report an interesting case of a chronic "ileo-caecocolique invagination." It is mentioned here because of the careful histologic study made and on account of their interpretation of the pathologic findings. The specimen described was removed from a young Arab at operation and consisted of the cecum, a portion of the ileum, and a portion of the ascending colon. Three areas of ulceration were noted in the cecum and are described as resembling dysenteric (dysentériques) ulcers, though none of the specific pathogens that produce the more frequent forms of infectious ulcerative intestinal lesions are demonstrated. The ulcers present nothing unusual, there being a central loss of substance with a surrounding subacute inflammatory reaction, and they are sufficiently deep to involve the muscularis. The intestinal wall intervening between those three discrete areas of ulceration is not noteworthy except for some edema. The authors draw particular attention to the plexuses of Auerbach and Meissner, showing that except where directly involved in the ulcerations or their dense surrounding inflammatory reaction, the plexuses are histologically normal. Sections of the ileum and ascending colon are not noteworthy, except for some edema and hyaline change in the ileum. This case of Masson and Leriche is lengthily recited because the authors consider the cecal ulcerations as the primary factors in the chronology of events: to quote "*Que les ulcerations dysentériques doivent être considérées comme primitives.*" The histopathology of the lesions they described differs from our case and that of Cole's in that their lesions have been of longer duration, with ulceration and evidence of beginning organization in the surrounding inflammatory zones, as indicated by the formation of new capillaries, etc. We feel that the lesion described by us, if encountered at a later date, would also have shown a loss of substance in the zone occupied by the necrotic material and that evidence of tissue repair would undoubtedly have been demonstrable at a later stage. In brief, the difference appears to be one of degree and not of quality.

In a brief consideration of the theories regarding the physiologic pathology of intestinal intussusception in the absence of tumors, diverticula, etc., two often quoted opposing schools may be regarded: one attributing the beginning of an intussusception to a primary localized area of intestinal spasm, the other to a primary area of intestinal paraly-

17. Masson, P., and Leriche, R.: *Recherches sur la physiologie pathologique de l'invagination intestinale chronique*, Lyon chir. 16:325-343 (May-June) 1920.

sis. Nothnagel¹⁸ is probably the most vigorous proponent of the former theory while Peyer (quoted by Kasemeyer¹⁹ and Leubuscher²⁰) and Leichtenstern²¹ espouse the latter hypothesis, which is the older. Both Nothnagel and Leubuscher have been unable to demonstrate experimentally the paralytic mechanism of intestinal invagination. On the other hand, Nothnagel by the use of the faradic current on the rabbit intestine has produced a tetanic contraction of a circumscribed portion of intestine. At the point where the contracted intestine and the caudad normal portion join, Nothnagel noted a small invagination formed by the normal distal segment of the intestine drawing itself up over the distal portion of the contracted portion in an umbrella-like manner. The further formation of the invagination occurred at the expense of the distal segment of intestine. Nothnagel feels that after the invagination is well developed the tip of the intussusception, which is then well in confines of the distal intestinal segment, acts as any other intestinal content, exciting peristalsis and causing propulsion of the intussusceptum analward. In this regard it may be mentioned that Treves (quoted by Nothnagel) accepts Nothnagel's view and a case reported by Rushmore² in a child of 9 also confirms in part this explanation. Operation on Rushmore's patient disclosed a well developed intestinal intussusception. After partial reduction had been effected manual traction was interrupted for a moment. In this interval Rushmore noticed that the intussusception began to reform by the intussusciens sliding up over the intussusceptum instead of the intussusceptum gliding down into the intussusciens as is usually regarded as the mechanism.

A case reported by Veau²² would also seem to bear out in part Nothnagel's theory clinically. Veau's case occurred in a male infant of 5 months on whom he had operated for an intussusception by resecting the cecum. Thirty-six hours after operation the patient again began to develop symptoms of intestinal obstruction. At the second operation Veau found about 50 cm. of the small intestine tightly contracted and firm. During this observation the author saw two invaginations of about 1 cm. occur at either end of the constricted intestine, but he does not describe their mechanism. He concludes, however, that spastic contraction is essential before intussusception can occur.

18. Nothnagel, H.: *Specielle Pathologie und Therapie*, Vienna, A. Holder, 1903, 17:385-417.

19. Kasemeyer, E.: *Tumorinvagination des darms*, *Deutsche Ztschr. f. Chir.* 118:205-264, 1912.

20. Leubuscher, G.: *Experimentelle beiträge zur aetiologie der darm-invagination*, *Virchows Arch. f. path. Anat.* 85:83-94, 1881.

21. Leichtenstern, O.: *Ueber darm-invagination*, *Prager Vierteljahrschr. i. prakt. Heilk.* 2:189-221; 4:58, 1873.

22. Veau, V.: *Le spasme intestinal comme cause d'invagination*, *Bull. Soc. de pédiat. de Paris* 8:424-428, 1906.

The production of reversed intestinal peristalsis by the use of sodium carbonate²³ is also confirmatory of Nothnagel's observation. The application of sodium carbonate to the serous aspect of the intestine produces, according to Morris, a pronounced tonic spasm followed by intussusception of the contracted portion by reverse peristalsis of the caudad lying intestine.

A suggestive experimental observation has recently been made by Alvarez²⁴ in the small intestine of the cat showing how antiperistalsis may occur without explainable cause. The observance of antiperistalsis with obstruction is, of course, not uncommon, while in the large intestine its occurrence without obstruction is physiologic.

There are, of course, other subscribers to the spasmodic theory, principally Brinton and Rafinesque (quoted by Nothnagel), who explain the further development of the intussusception in a somewhat different manner.

Peyer and Leichtenstern, while both embracing the hypothesis that a primary zone of intestinal paralysis is the preliminary requirement before intussusception can occur, nevertheless differ as to the process whereby the intussusceptum and intussusciens form. The details of this are probably irrelevant to this discussion. A recent clinical instance that is construed as supporting the paralytic theory of intussusception formation is reported by Syring.²⁵ This author reports a case of intussusception observed during the recent World War in a soldier with a gunshot wound of the abdomen. Operation revealed, in addition to several intestinal perforations, an injury to the mesentery of the jejunum. At the exact level of the mesenteric injury the operator noted a complete intussusception, 8 cm. long, easily reduced and covered with a layer of fibrin. Syring feels that the mesenteric injury severed a branch of the superior mesenteric artery and an accompanying nerve, a branch of the superior mesenteric plexus, in this way depriving this segment of intestine of its vagus innervation and possibly also of its splanchnic nerve supply. This series of events the author feels caused a localized area of intestinal paralysis, thereby fulfilling the primary requirement for the formation of the intussusception which he discovered at operation.

We feel that the case reported in this article is an instance of partial cecal intussusception occurring in a portion of the cecum where, if one

23. Morris, R. T.: The Production of Ileal Intussusception with Carbonate of Sodium, *M. Rec.* 45:389, 1894.

24. Alvarez, W. C., and Mahoney, L. J.: Peristaltic Rush in the Rabbit, *Am. J. Physiol.* 69:211-225 (July) 1924.

25. Syring: Ein Beitrag zur nervenpathologie des darmes und zur pathogenese der intussuszeption, *Beitr. z. klin. Chir.* 114:131-137, 1918.

may judge from the literature, cecal intussusceptions are prone to originate.

The formation of the invagination in this particular instance, we assume, is best explained by the occurrence of abnormal intestinal excitation following the ingestion of some ipecac, which in turn caused severe and ineffectual attempts to vomit. As part of the intestinal reaction an area in the cecum underwent abnormally prolonged contraction so that when relaxation did occur a portion of the contracted intestine had undergone a localized edema, due to some degree of circulatory stasis. In this way an invagination persisted and its spontaneous reduction was no longer possible. After this primary invagination and edema, the invaginated portion acted much as a foreign body; it excited intestinal peristalsis with consequent traction on the invaginated area which resulted in further circulatory embarrassment, finally producing at the apex of the invaginated portion an area showing the varying degrees of damage that may follow a prolonged ischemia. This is well brought out in part of figure 3 where the mucosa, muscularis mucosae and the superficial portion of the submucosa form a structureless necrotic area. Peripheral to this, in addition to the inflammatory reaction one sees the remaining submucosa very edematous and both layers of the tunica muscularis show definite degeneration, as evidenced by loss of cell outline and the impaired staining reaction of their component muscle fibers as previously described. The whole picture in fact is similar to some of the pathologic appearances first described by D'Arcy Power²⁶ in his article on the minute anatomy of intussusception.

The normal appearance of the ileum and all other portions of the large intestine rather speak against their participation in this process. To fulfil Leichtenstern's hypothesis one should have sufficient intestine proximal to the invaginated area, which would represent the segment of paralyzed intestine, to propel the latter into the caudad intestinal segment.

Obviously the cecum without the ileum could not afford this propelling force, owing to the situation of the invagination. There is no evidence that the ileum supplied this want for there is nothing to indicate an ileocecal invagination, which would have been necessary to allow the remaining proximal portion of the cecum to participate.

Reverting to Nothnagel's explanation of intussusception in the absence of tumors and diverticula, we feel that in our case his first postulate has probably been fulfilled; namely, an area of intestinal spasm has most likely occurred. Whether the caudad segment of large intestine drew itself up over this area of constriction one cannot say.

26. Power, D'Arcy: Some Points in the Minute Anatomy of Intussusception, *J. Path. & Bact.*, June, 1897.

It does not, however, seem probable that a portion of the circumference of the intestine would undergo antiperistalsis in such a manner as to provide an invagination such as this, for intestinal movement is usually circumferential even when antiperistaltic. However, at operation nothing could be noted that might suggest a participation of the neighboring large intestine in an intussusception. Indeed, the remainder of the circumference of the cecum at the level of the invagination appeared normal. We therefore feel that we are in the presence of an incomplete and probably incipient form of cecal invagination which represents one of the early stages of more advanced forms of cecal intussusception reported in the literature as arising in this particular situation; that is, near the point of convergence of the anterior and lateral taeniae coli. From pathologic evidence at hand we believe that an unusual contraction of the wall of the cecum in this particular segment provided the beginning for a series of events resulting in the invagination described. Furthermore, it seems reasonable to assume that this may have occurred without participation of the distal lying segment of the intestine as postulated by Nothnagel, or by a mechanism such as that described by Leichtenstern.

One naturally wonders whether processes such as that observed in this case, possibly not even so far advanced, are not of more frequent occurrence than is generally supposed. In fact, it is possible that such conditions unless carefully searched for may be overlooked at operation, the condition correcting itself through manipulation and the subsequent freedom from symptoms attributed to the removal of a macroscopically "suspicious looking" but a histologically normal appendix.

3. Cases in which apparently free omentum twists without being the site of a mass or being adherent in the pelvis. Payr⁶ says that this variety presumably is due to the fact that the veins are larger and more tortuous than the arteries and that when the veins are compressed by a kink of some kind they become turgid and full of blood; the arteries form a tense cord about which the omentum turns and once started to twist

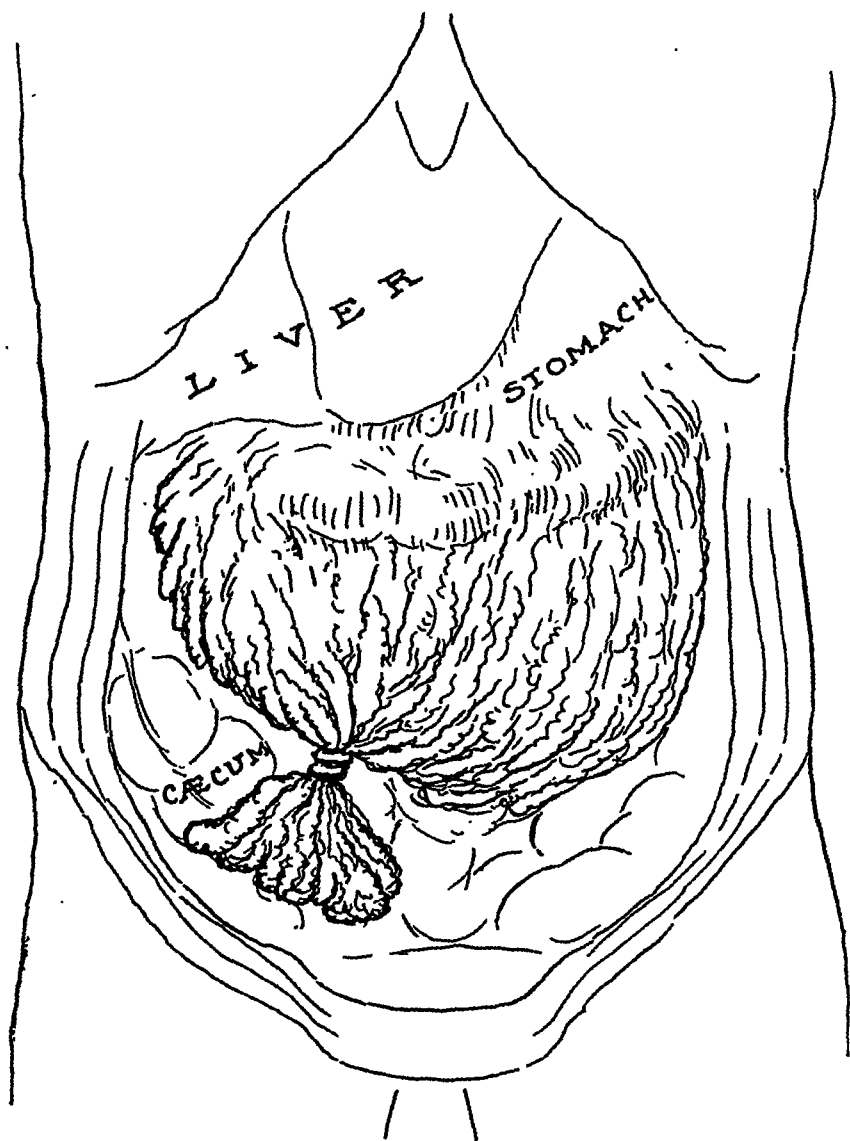


Fig. 1.—Torsion in the omentum (diagrammatic sketch).

continues with resulting obstruction to the circulation and subsequent gangrene. The following case belongs to group 3 as no etiologic factor was found to explain the torsion. There was no evidence of hernia or pelvic infection, and the appendix showed no macroscopic evidence of

6. Payr: *Arch. f. klin. Chir.* 67, 1902.

disease. The patient had a chronic cholecystitis and cholelithiasis but there were no adhesions or bands in the upper part of the abdomen. Figure 1 is a diagrammatic sketch of the torsion in the omentum. Figure 2 shows three complete twists in the omentum.

REPORT OF CASE

A woman, aged 28, had had pains in the abdomen for eighteen hours. She had had no serious illnesses or surgical operations; two children, aged 6 and 4

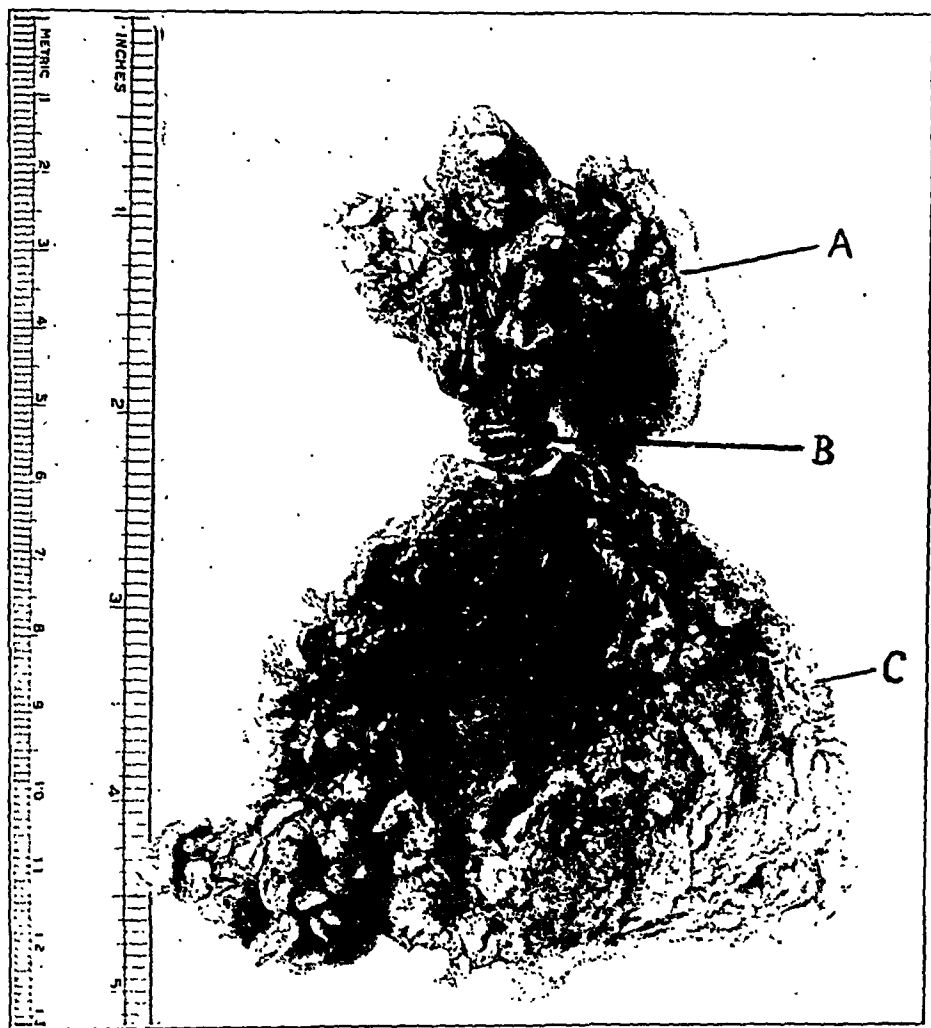


Fig. 2.—*A*, normal omentum; *B*, three twists in omentum; *C*, gangrenous omentum.

years, were alive and well. She had no puerperal infection. She had been bothered with indigestion and vague pains in the upper part of the abdomen after eating for several years. This pain was different from the one she was complaining of at the present time. She attributed it to an affected gallbladder and gallstones, as her husband had the same symptoms, for which he had an operation.

Her menstrual periods were regular and came every twenty-eight days. The last period had been two weeks before admission.

The patient stated that eighteen hours before admission she was seized with pains in the region of the umbilicus and that after a few hours she vomited. The pain later became localized to the right lower quadrant. It was severe enough to keep her awake most of the night. A doctor was called eight hours after the onset of the pain and diagnosed her condition as acute appendicitis. An operation was advised. The patient was out of town and refused as she preferred to return home. The pain continued but chiefly in the right lower quadrant, at which place she complained of considerable tenderness.

Physical examination showed a woman confined to bed apparently suffering from acute pain in the abdomen. The temperature was 99, the pulse 80. The throat was negative for tonsillitis or pharyngitis. The chest was normal. On abdominal examination there was no tenderness over the left or the right upper quadrant. There was a marked tenderness over the right lower quadrant at McBurney's point and a slight rigidity in this region. The tenderness seemed out of proportion to the pain of which she complained. There was no costo-vertebral tenderness on either side. Vaginal examination showed the fornices normal. No masses were felt. The uterus was normal.

Urinalysis was negative. The leukocyte count was 17,000; polymorphonuclear neutrophils, 74 per cent; small lymphocytes, 19 per cent; large lymphocytes, 5 per cent, and transitionals, 2 per cent.

The preoperative diagnosis was acute appendicitis.

The abdomen was opened through a right rectus incision, under ether anesthesia. When the peritoneum was opened, the hand was inserted to the right lower quadrant and a mass containing gangrenous omentum was encountered and delivered. This was not inspected carefully but was wrapped in abdominal pads. The cecum was then delivered and the appendix showed no evidence of acute infection. An appendectomy was performed, the stump of the appendix being carbolized and inverted. The upper part of the abdomen was palpated and the gallbladder was found to contain one large stone. The omentum was then inspected and it was found to have the lower portion twisted on itself three times. No masses were felt in the omentum. The mass of gangrenous omentum was then excised, about 1 inch (2.5 cm.) of healthy omentum above the twist being removed. The incision was enlarged upward and the gallbladder was found to contain one large stone, with no evidence of acute infection. A cholecystectomy was performed. The common duct was negative for calculi. A rubber tissue drain was inserted to the space in front of the right kidney, known as Morrison's space, and the abdomen was closed in layers.

The pathologic report stated that the gross specimen measured 110 by 90 mm. It was twisted in the middle. The lower part was hemorrhagic. Microscopic examination of the sections showed fat tissue that was hemorrhagic. The blood vessels were engorged and partly thrombosed, with slight infiltration of the fat tissue by polymorphonuclear leukocytes.

The patient made an uneventful recovery and was discharged from the hospital on the twelfth day.

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THE VALVES OF HEISTER*

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In 1732 Laurentius Heister¹ first described the valvular arrangement of the mucous membrane of the cystic duct that bears his name. He attributed to these leaflets projecting into the cystic duct a functional rôle of the gallbladder, namely, the storage of bile. Recent studies are at variance with this hypothesis; for this reason I undertook an anatomic and experimental study of the problem in 1923.

The mucous folds in the cystic duct apparently reach their highest development in man. They are present in the dog, rabbit and a few other animals, but are less developed and fewer in number. A study of the comparative anatomy, therefore, suggests the very minor part played by these leaflets in the functional activity of the gallbladder. Indeed, in many species there are no leaflets and this must be considered in attempts to ascribe a functional rôle to the valves. Certainly their absence lessens the significance of any functional activity that might be credited to them in man. It does not seem likely that the valves of Heister are vestigial in man, for if they were the leaflets presumably would be better developed in the lower animal forms.

ANATOMY

The cystic duct in man is not of constant shape or size. It has been variously described as "kinked," "bassinet-shaped," "sharply flexed on itself," "S-shaped" and "double mesial curved" (figs. 1 and 2). In a series of 612 cystic ducts examined at necropsy, only nineteen were true S-shape; forty-one were single curves sharply flexed on themselves. In five instances, however, the duct was devoid of curves or flexions and appeared as a straight duct in gallbladder specimens free from gross pathologic changes (figs. 3 and 4).

Schmieden² has pointed out that in most cases the cystic duct leaves the gallbladder at the side and not at the most proximal portion of the

* Work done in the Section on Pathologic Anatomy, Mayo Clinic.

1. Heister, L., quoted by Schmieden, V.: Ueber die "Stauungsgallenblase," *Zentralbl. f. Chir.* 47:1257-1261, 1920.

2. Schmieden (footnote 1). Schmieden, F., and Rohde, Carl: Die Stauungsgallenblase mit besonderer Berücksichtigung der Ätiologie der Gallenstauungen, *Arch. f. klin. Chir.* 118:14-53, 1921.

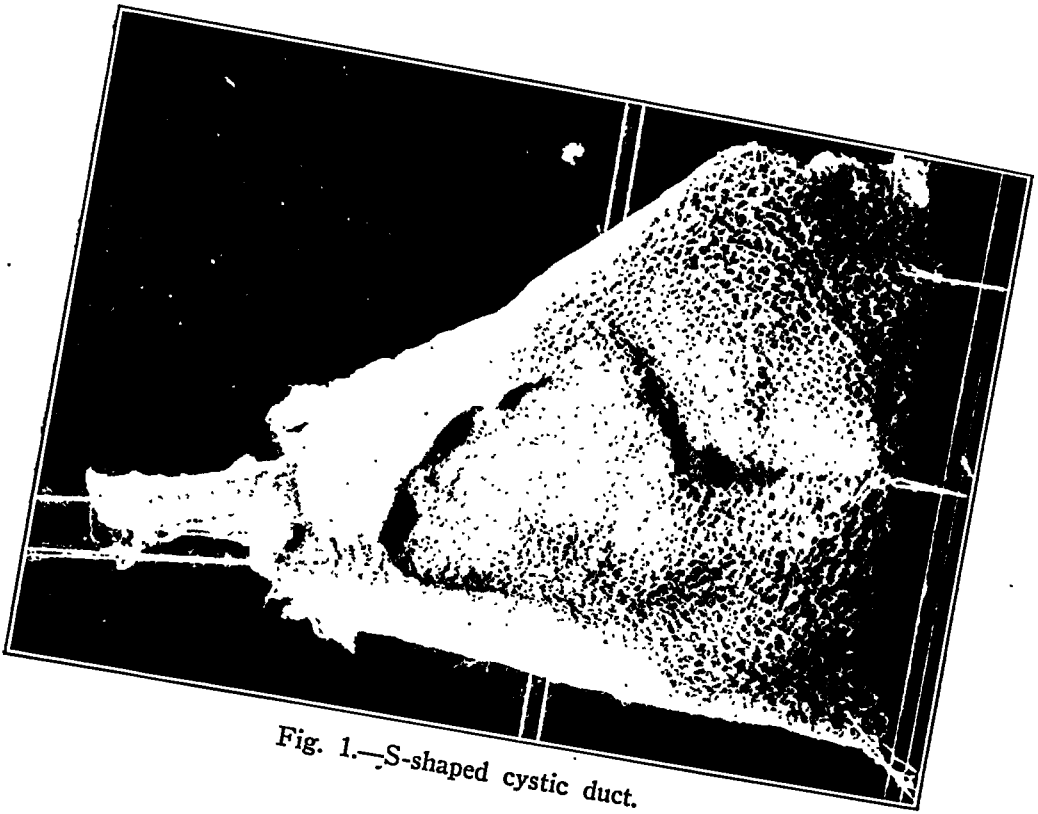


Fig. 1.—S-shaped cystic duct.

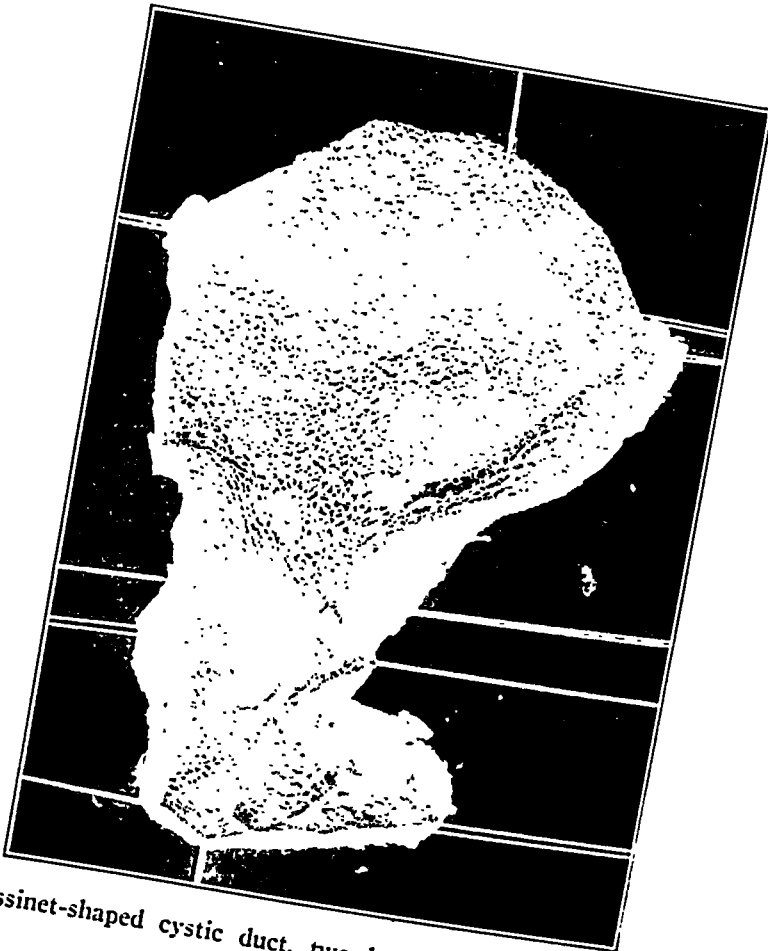


Fig. 2.—Bassinet-shaped cystic duct, two leaflets only constituting valves of Heister.

organ. I also observed this. Jacobson and Gydeson³ believe that the cystic kink, which is frequently present close to the emergence of the cystic duct from the gallbladder, is concerned in the emptying of the organ. They assert that the gallbladder can be distended almost to the



Fig. 3.—Straight cystic duct.



Fig. 4.—Straight cystic duct.

bursting point without forcing bile out of the cystic duct, whereas it can be easily emptied by slight longitudinal traction on the duct. They believe that the valvular action of the cystic kink is thereby lessened.

3. Jacobson, Conrad; and Gydeson, Carl: Function of the Gallbladder in Biliary Flow. *Arch. Surg.* 5:374-394 (Sept.) 1922.

German pathologists lay much emphasis on the stagnation of bile produced by this angulation of the cystic duct as an etiologic factor in the formation of gallstones. From my study I was led to believe that such mechanical causes of obstruction to the flow of bile must be relatively rare.



Fig. 5.—Valvular arrangement in cystic duct.

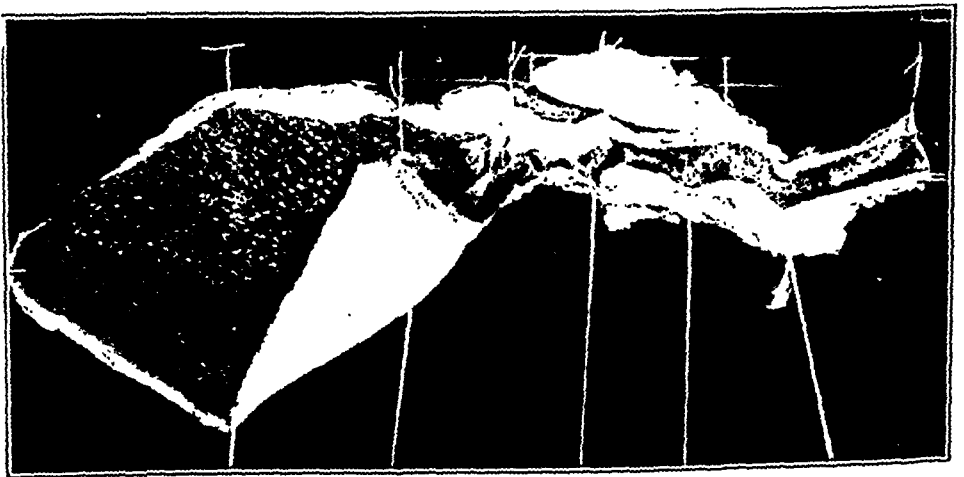


Fig. 6.—Cholesterosis of gallbladder, with no leaflets in lower two-thirds of cystic duct.

The valves of Heister are projections of mucous membrane into the lumen of the cystic duct. They line the course of the duct more or less completely, being larger and less numerous at the distal end and

smaller and more abundant at the common duct terminus of the cystic duct (fig. 5). There are, however, many variations in this distribution. In three of our series of 612 cases there were no leaflets in the lower third of the cystic duct (fig. 6). In one case the first leaflet began almost a fourth of the way up the gallbladder from the cystic duct.

The leaflets are arranged more or less spirally, running in a clockwise direction down the cystic duct from its origin at the gallbladder. The majority of the leaflets extend from one-half to three-quarters of the way around the duct. The leaflet above and below overlaps the intermediate valve to a greater or less extent. In many instances the leaflets make a complete circuit of the duct, and in several of the cases

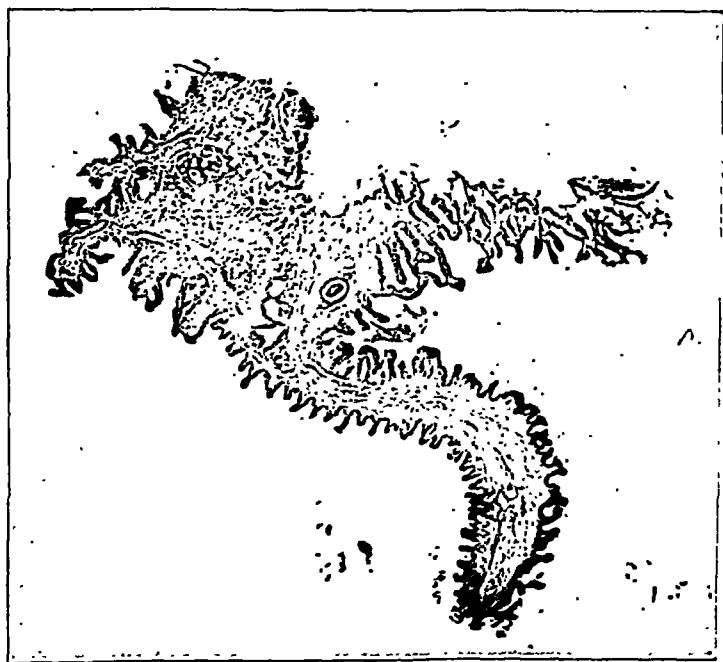


Fig. 7.—Section of leaflet of valves of Heister ($\times 15$).

in this study a single leaflet made two complete turns around the duct. Hartmann⁴ and Faure,⁵ in their early descriptions, pointed out that the duct is not a spiral canal, but that it is a duct interrupted by incomplete spiral leaflets in its course. They pointed out that the upper leaflets sometimes extend three-quarters of the way around the duct, and for this reason the duct is impassable to a probe or other solid object. Terrier and Dalley⁶ agreed with these contentions and made copper

4. Hartmann, quoted by Jacobson and Gydeson (footnote 3).

5. Faure, J. L., quoted by Jacobson and Gydeson (footnote 3).

6. Terrier, F., and Dally: Du cathétérisme des voies biliaires, *Rev. de chir.* 12:136-168, 1892.

models of the leaflets. Brewer⁷ likewise found the cystic duct impassable to a probe in all but ten of ninety-seven cases; I succeeded in passing a probe in only sixteen of 198 normal gallbladders. Of this number eight possessed no leaflets nor other suggestion of valves of Heister.

The number of leaflets comprising the valves varies greatly (table 1). In a series of 338 essentially normal gallbladders, in which there were no gross evidences of inflammatory changes and no gallstones or evi-

TABLE 1.—*Leaflets Comprising the Valves of Heister.*

| Normal Gallbladders | | Essentially Normal Gallbladders (Cholesterosis) | | |
|---------------------|-------|---|-------|-------|
| Leaflets | Cases | Leaflets | Cases | Total |
| .. | 8 | .. | .. | 8 |
| 1 | 5 | 1 | .. | 5 |
| 2 | 13 | 2 | 4 | 17 |
| 3 | 29 | 3 | 10 | 39 |
| 4 | 30 | 4 | 41 | 71 |
| 5 | 34 | 5 | 31 | 65 |
| 6 | 28 | 6 | 14 | 42 |
| 7 | 20 | 7 | 14 | 34 |
| 8 | 10 | 8 | 6 | 16 |
| 9 | 13 | 9 | 7 | 20 |
| 10 | 2 | 10 | 6 | 8 |
| 11 | 1 | 11 | 4 | 5 |
| 12 | .. | 12 | 3 | 3 |
| 13 | 2 | 13 | .. | 2 |
| 14 | 1 | 14 | .. | 1 |
| 17 | 1 | 17 | .. | 1 |
| 22 | 1 | 22 | .. | 1 |
| | 198 | | 140 | 338 |

TABLE 2.—*Spiral Leaflets in the Valves of Heister*

| | | Cases | | | | | | | | | | | | | | | | |
|-----------------------------------|-------|-------|----|----|----|----|----|----|----|----|----|----|----|-----|-----|-----|-----|--|
| Leaflets | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 17 | 22 | |
| Spirals | | | | | | | | | | | | | | | | | | |
| 1 | | .. | .. | .. | 7 | 6 | 11 | 7 | 4 | 6 | 2 | 1 | .. | 1 | ... | ... | ... | |
| 2 | | .. | .. | .. | 3 | 4 | 6 | 3 | 5 | 8 | 4 | 2 | 3 | ... | ... | ... | ... | |
| 3 | | .. | .. | .. | .. | 1 | 1 | .. | .. | .. | .. | .. | .. | 1 | 1 | ... | 1 | |
| 4 | | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | ... | |
| Total spirals..... | | .. | .. | .. | 10 | 11 | 18 | 10 | 9 | 14 | 6 | 3 | 3 | 2 | 1 | 1 | 1 | |
| Total cases..... | | 6 | 23 | 51 | 86 | 76 | 55 | 29 | 21 | 24 | 8 | 5 | 4 | 2 | 1 | 1 | 1 | |
| Spirals, percentage of total..... | | .. | .. | .. | 11 | 14 | 32 | 33 | 42 | 58 | 75 | 60 | 75 | 100 | 100 | 100 | 100 | |

dence of their previous existence, the leaflets varied from one to twenty-two in number. In eight instances in this normal group no leaflets were demonstrable grossly. This seems significant for it is not unusual to note the absence of leaflets in cases of cholelithiasis, as was noted in six of 123 cases. But their absence from specimens free from disease suggests that these ducts probably never possessed any valves. Terrier and Dally have likewise noted the absence of valves of Heister, but it is not

7. Brewer, G. E.: Preliminary Report on the Surgical Anatomy of the Gall-bladder and Ducts from an Analysis of One Hundred Dissections, *Ann. Surg.* 29: 721-730, 1899.

certain that previous disease did not exist in their cases. If one wishes to ascribe any functional purpose to these valves one must be able to correlate their absence in man and in the lower forms of life with that function.

I was unable to find any uniformity in the arrangement of the leaflets. In most specimens the leaflets ran in a spiral, clockwise manner, partially encircling the cystic duct and mortising between the leaflets on the opposite wall of the duct. In some instances the leaflets were not spiral (table 2), and in others they extended more than one-half to

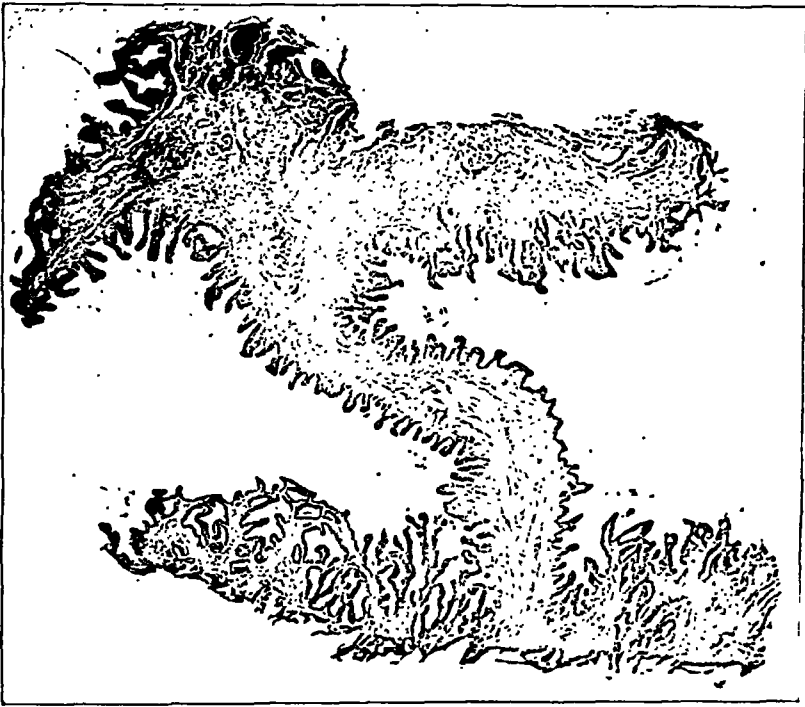


Fig. 8.—Section of valve of Heister between walls of cystic duct ($\times 15$).

three-quarters of the way around the duct, did not mortise into the space between the leaflets on the opposite side of the duct and frequently ran in a counterclockwise manner. In a particularly interesting specimen, having seventeen leaflets in the valves of Heister, I was able to demonstrate all of these variations. It seems significant that, in fourteen of the 338 normal gallbladder specimens, more than one leaflet ran in a counterclockwise manner.

From an anatomic point of view, therefore, it appears that the valves of Heister must be ineffectual in completely obstructing the flow of bile in either direction in the cystic duct. Moreover, whatever their function in the biliary system, it cannot be an essential one, as in eight instances no valves were present although the gallbladder was presumably normal.

HISTOLOGY

The valves of Heister are essentially projections of the mucosa at the outlet of the gallbladder arranged in a valvular manner. The epithelium is of the same tall columnar type, arranged in rugae of delicate branching forms, identical with those comprising the gallbladder mucosa. The mucosa of the cystic duct is similar to that of the gallbladder and the common duct, less intricate than the former and more

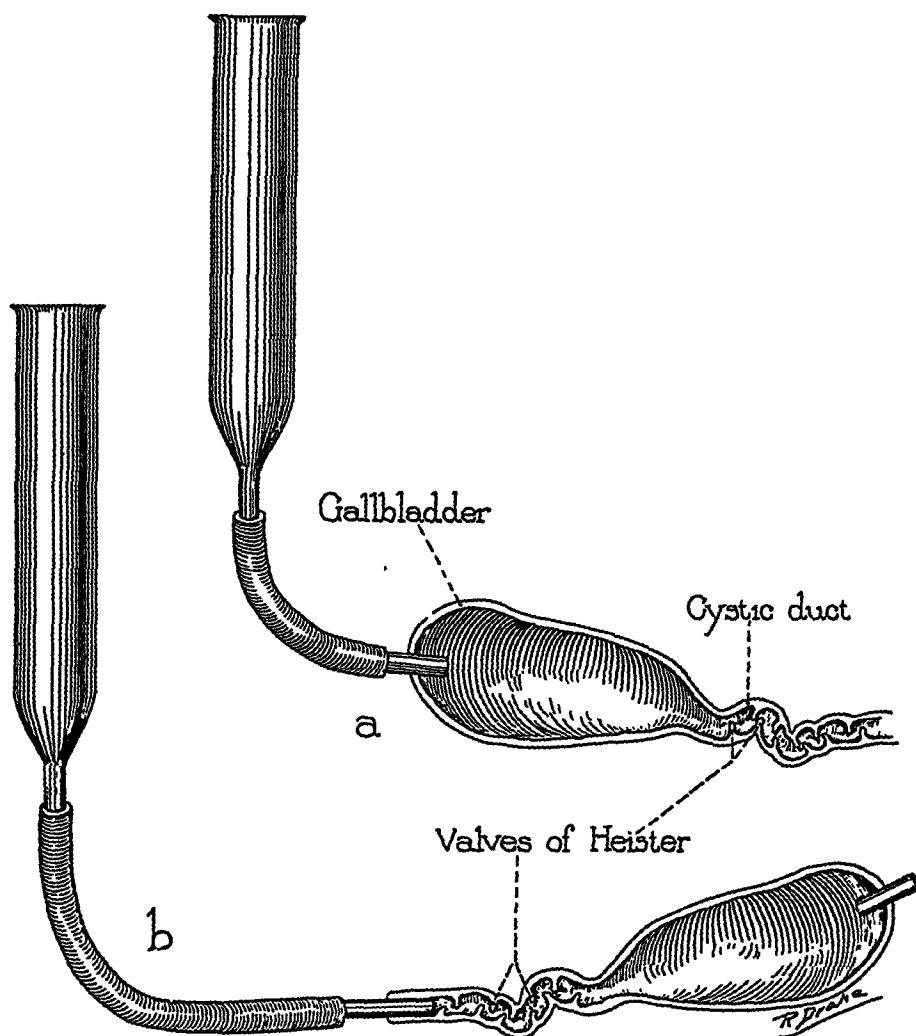


Fig. 9.—*A*, passage of fluid proximally; *b*, passage of fluid distally through cystic duct.

delicate than the latter. Its structure suggests a functional activity similar to that of the gallbladder; indeed, it is not difficult to believe that the mucosa of the cystic duct may be able to absorb fluids and probably lipoids almost as readily as the mucosa of the gallbladder comparable to that previously demonstrated.⁸

8. Mentzer, S. H.: Cholesterosis of the Gallbladder, *Am. J. Path.* 1:383-388 (July) 1925.

The cystic duct is composed of smooth muscle fibers running in three directions, in a manner comparable to that in the wall of the gallbladder. The musculature of the valves of Heister has been the subject of considerable study, and some authors doubt the presence of longitudinal fibers in the leaflets. These, however, may be seen in any freshly prepared specimen on serial section (fig. 7). The circular smooth muscle fibers constitute the bulk of muscle in the leaflets themselves, and are, apparently, a continuation of the circular fibers of the cystic duct (fig. 8). I have not been able to demonstrate any sphincter arrangement of circular fibers at the terminal end of the cystic duct. Indeed, the duct was patent in all of the specimens, and a probe could be easily passed through it; it is not until the probe reaches the first leaflets that obstruction is met with.

The subserosal fat layer is relatively thick, as it is in the wall of the gallbladder. The serosal layer is thin and composed of squamous cells.

PHYSIOLOGY

Heister believed that the valves were placed in the cystic duct for the purpose of storing bile in the gallbladder until such time as the body needed it. This anthropomorphic view is held even now; it is, in fact, part of the accepted theory of the function of the gallbladder. Lyon's⁹ application of Meltzer's law of contrary innervation of the gallbladder explained the opening of the valves of Heister to permit the passage of bile into the common duct. Schmieden² believes that the valves had something to do with the emptying of the gallbladder. Haberland,¹⁰ Winkelstein and Aschner¹¹ believe the respiratory squeeze is sufficient to express bile from the gallbladder and past the valves of Heister into the common duct. Barker,¹² in 1907, expressed the belief in a unique function of the valves; namely, that the gallbladder secreted mucus at the rate of about two ounces a day but that this secretion was too viscid to pass down the cystic duct and, therefore, when the body needed the secretion the valves of Heister opened to permit bile to enter the gallbladder from the hepatic ducts, to dilute the viscous secretion, so that it could pass readily down the cystic duct. When the gallbladder secretion was no longer needed by the body the valves would close. He stated that there are ten of these valves to effect such closure.

9. Lyon, B. B. V.: *Diagnosis and Treatment of Diseases of the Gallbladder and Biliary Ducts*, J. A. M. A. **73**:980-982 (Sept. 27) 1919.

10. Haberland, H. F. O.: *Studien an den Gallenwegen*, III, Die Funktion der Gallenblase, Arch. f. klin. Chir. **130**:625-646, 1924.

11. Winkelstein, A., and Aschner, P. W.: *Experimental Studies on Entrance of Bile Into Duodenum*, Am. J. M. Sc. **169**:679-686 (May) 1925.

12. Barker, M. R.: *What Is the Function of the Gallbladder? And Why the Folds of Heister in the Cystic Duct?* Med. Rec. **72**:555-558, 1907.

Sweet,¹³ in 1924, suggested that the valves of Heister prevented the egress of bile from the gallbladder, that bile once in the gallbladder never left it by way of the cystic duct. As my anatomic studies did not help me to understand either of these contrary views, I undertook the following experimental study.

Twenty-two normal gallbladders with their attached cystic and common ducts were tested for the patency of their cystic ducts. One end of the common duct was ligated; to the other end was fastened a pipet whose smallest bore measured 3 mm. (the size of a small cystic duct). The pipet was connected with a measuring funnel and the latter filled with 25 cc. of glucose solution of varying strengths. The funnel was raised 30 cm. above the level of the gallbladder so that gravity flow forced the solution through the cystic duct and into the gallbladder (fig. 9). The time required for the passage was noted in each instance. In none of the twenty-two specimens was there complete obstruction to the

TABLE 3.—*Time Required for Passage of Glucose Solutions Through the Cystic Duct, Minutes*

| | | | | | | | | | | | | | | | | | | | | | | | |
|--------------------------------|-----|-----|---|-----|---|----|-----|-----|----|------|-----|----|-----|----|----|----|-----|----|----|----|----|---|-----|
| Glucose solution, 85 per cent | In | 5 | 4 | 9 | 3 | 11 | 4 | 8 | 13 | 10 | 5 | 7 | 14 | 8 | 17 | 10 | 6 | 15 | 9 | 7 | 12 | 6 | 8 |
| | Out | 4.5 | 5 | 7.5 | 4 | 10 | 6 | 7 | 14 | 11 | 7 | 5 | 12 | 7 | 15 | 8 | 6 | 13 | 11 | 6 | 13 | 5 | 9 |
| Glucose solution, 50 per cent | In | 3 | 3 | 6 | 2 | 8 | 3 | 6 | 10 | 7 | 4 | 5 | 10 | 6 | 12 | 7 | 4 | 11 | 6 | 4 | 8 | 5 | 5.5 |
| | Out | 3.5 | 4 | 5 | 3 | 7 | 5 | 5.5 | 11 | 8 | 5.5 | 4 | 7.5 | 5 | 9 | 5 | 3.5 | 8 | 7 | 4 | 9 | 4 | 5 |
| Glucose solution, 110 per cent | In | 8 | 6 | 12 | 5 | 14 | 6.5 | 11 | 16 | 14.5 | 8 | 10 | 17 | 11 | 21 | 14 | 8 | 18 | 12 | 10 | 15 | 7 | 11 |
| | Out | 7 | 7 | 10 | 6 | 12 | 8 | 8.5 | 18 | 15 | 8.5 | 7 | 16 | 10 | 18 | 11 | 7 | 16 | 14 | 9 | 13 | 9 | 12 |

flow of the solutions. The time required for the passage varied, from three minutes in one instance to seventeen in another (table 3). Obviously, the number of leaflets comprising the valves of Heister, the diameter of the cystic duct and its tortuosity were the determining factors in the time element. Solutions of approximately one-half and twice the viscosity of normal bile were then used, and in every instance they passed through the cystic duct.

Similar experiments were conducted on the same twenty-two specimens to determine the patency of the cystic duct in the opposite direction. The apparatus was connected with the fundus of the gallbladder so that solutions passed through the cystic duct into the common duct (fig. 9). The conditions for the experiments were identical except for the reversal of the direction of flow of the fluids. In this series also, there was no instance of obstruction to the flow of the glucose solutions, and there was no material change in the rate of flow of identical solutions in either direction through the cystic duct (table 3). In one instance it required five minutes for 25 cc. of the glucose solution of "normal" viscosity to

13. Sweet, J. E.: The Gallbladder: Its Past, Present and Future, *Internat. Clin.* 1:187-226 (March) 1924.

pass through the cystic duct from the common duct end, whereas seven minutes were consumed in passing in the opposite direction. But in five instances when glucose of like viscosity was used, less time was required for the passage from the gallbladder into the common duct compared to that in the opposite direction (table 3). In the remaining sixteen cases the rate of passage was essentially the same in either direction. Therefore, it was not possible to show any material change in the rate of flow of solutions in opposite directions through the cystic duct.

These experiments were handicapped from two standpoints, and therefore the data obtained are of suggestive value only. First, the specimens were obtained at necropsy, none later than eight hours after death. However, muscle tonus was gone. In vivo, muscle tone must play a part in the activity of the valves, even though it is slight. Second, the work is subject to error consequent on removal of the specimen *ex situ*. The cystic kink, although present in only a small proportion of the series (5 per cent), is altered in the operative manipulation.

Verification of the experiment might be made on the intact dog but this would not be wholly satisfactory since the dog's valves have but few and small leaflets.

PATHOLOGY

That the leaflets of the valves of Heister are concerned in disease of the gallbladder is obvious in any study of cholelithiasis. In seven of a series of 612 postmortem examinations inspissated bile was found packed in the leaflets and gallstones were found in seventeen. Such obstructions play a part in hydrops and probably in many cases of empyema of the gallbladder. Inspissated bile alone, when packed in the leaflets of the cystic duct, may produce sufficient obstruction to check the flow of bile from the gallbladder; thus the bile becomes excessively concentrated with probable change in the relative content of bile salt. In such event a change in the acidity of the bile would occur, and, according to Lichtwitz's¹⁴ theory of the formation of gallstones, the ideal conditions for biliary calculi would be present.

Naunyn¹⁵ has emphasized the part stasis of bile plays in the formation of gallstones, as produced by mechanical obstruction from kinking of the cystic duct, or by actual blockage of the duct itself. Schmieden believes that kinking of the duct alone, without inflammatory or obstructive changes, is sufficient to cause severe colic in the area of the gallbladder.

14. Lichtwitz, L.: Experimentelle Untersuchungen über die Bildung von Niederschlägen in der Galle. *Deutsches Arch. f. klin. Med.* **92**:100-103, 1907.

15. Naunyn, B.: Zur Lehre vom Aufbau und Umbau der Gallensteine, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **37**:545-550, 1924.

CONCLUSIONS

1. There are two contrary views with regard to the function of the valves of Heister; they are (*a*) that the valves aid in the storage of bile in the gallbladder until digestive demands require its egress from the gallbladder, and (*b*) that once bile has entered the gallbladder the valves prevent it from leaving by way of the cystic duct. Anatomic study of the valves does not favor either hypothesis.

2. A study of necropsy specimens showed that solutions passed in either direction through the cystic duct with equal facility.

3. The functional activities of the valves of Heister cannot be very important, since the majority of animals do not possess the valves or their functional equivalent. Moreover, eight normal gallbladder specimens from human beings examined at necropsy were without leaflets or indications of their having existed.

4. The study suggests that the valves of Heister check the rapid passage of bile into or out of the gallbladder, presumably so that bile in the gallbladder may remain at a relatively uniform consistency. If such is the function of the valves they aid in maintaining the gallbladder as a uniform sampling organ of bile, as suggested by Mann.¹⁶

16. Mann, F. C.: The Functions of the Gallbladder, *Physiol. Rev.* 4:251-273 (April) 1924.

BRITTLE BONES AND BLUE SCLERA

HEREDITARY HYPOPLASIA OF THE MESENCHYME *

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ST. LOUIS

1. INTRODUCTION

Having had under treatment a typical case of that type of fragilitas ossium which is commonly called "brittle bones and blue sclera," I am in a position to describe for the first time the pathology of the condition, and to add certain clinical observations to those which are included in the rather extensive literature on the subject.

The term "fragilitas ossium" is loosely applied to conditions that are characterized by an abnormal fragility of the bones. Bone fragility may be congenital or acquired, and may be due to developmental defects or to local or general absorption of the mineral constituents of normal bone. It is one of the most obscure subjects in modern medicine. The terminology is confused and the pathology is not well understood.

Our knowledge is particularly vague in regard to the so-called idiopathic or developmental types of bone fragility. This includes three fairly well defined clinical conditions: (1) osteopsathyrosis, described by Lobstein in 1833 as a definite clinical entity; (2) osteogenesis imperfecta, described by Vrolik in 1849 as a separate condition, and (3) the syndrome of brittle bones and blue sclera, described by Spurway¹ in 1894.

Hundreds of articles have been written on fragilitas ossium in general and the foregoing conditions in particular, but it is still a question whether or not they are all merely different terms for one condition. In regard to osteogenesis imperfecta and idiopathic osteopsathyrosis, Looser² prefers to call them osteopsathyrosis congenita and tarda, holding that in each the pathologic process is the same, the only difference being that in the former the fractures are present at birth while in the latter the fractures occur in infancy or childhood. Somewhat similar views are held by Sumita,³ Bauer⁴ and others who have recently studied the pathology of the first two types of fragilitas ossium.

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1. Spurway, J.: Hereditary Tendency to Fracture, Brit. M. J. 2:845, 1896.

2. Looser, E.: Zur Kenntniss der Osteogenesis Imperfecta congenita et tarda, Mitt. a. d. Grenzgeb. d. Med. u. Chir. 15:161, 1906.

3. Sumita, M.: Beitrage zur Lehre von der Chondrodystrophia foetalis und Osteogenesis imperfecta, Deutsche Ztschr. f. Chir. 107:1, 1910.

4. Bauer, K. H.: Ueber Identität und Wesen der Sogenannten Osteopsathyrosis und Osteogenesis imperfecta, Deutsche Ztschr. f. Chir. 160:289, 1920.

In regard to the third type which is associated with blue sclera, the pathology is largely unknown as Bronson's⁵ description of the structure of the sclerotic coat of an eye from a case of brittle bones and blue sclera is the only report on the pathology of any of the tissues which I have been able to find in the literature. Not only is the pathology unknown but descriptions of the various clinical aspects of the condition are scattered through a rather extensive literature and it is only with difficulty that one is able to obtain a comprehensive clinical picture of the syndrome.

In our case we have roentgenograms of the entire skeleton and microscopic sections of the bone, tendon, muscle and skin from material removed at operation. We have determined the basal metabolism, studied the blood chemistry, and have also obtained the total phosphorus, calcium and nitrogen balance over two six day periods. The chemical analyses are being made by Dr. Ethel Ronzoni and will be reported in a later article.

From our own observations and an analysis of the cases reported in the literature we are able to describe a clear cut clinical syndrome which we shall term hereditary hypoplasia of the mesenchyme. The most prominent feature of the condition is that the sclerae of the affected persons appear to be china blue in color and that the blue sclerae are transmitted as a dominant hereditary characteristic. Many of the affected persons are afflicted with fragilitas ossium, hereditary deafness and hypermotility of the joints. All of the abnormalities seem to be due to defects in the development of some of the tissues which arise from the mesenchyme.

In this article we are not especially concerned with the possible identity of the various types of fragilitas ossium, but shall endeavor to give as completely as our present knowledge permits the clinical and pathologic picture of the condition which we call hereditary hypoplasia of the mesenchyme. As the condition is a very complex one it seems best to consider it under the following headings: history, report of case, heredity, physical characteristics, the eyes, deafness, fractures, deformities, conditions of the joints and muscles, roentgenographic appearance of the bones, pathology, other abnormalities, laboratory findings, comment and summary.

2. HISTORY

Blue sclera was first described by Von Ammon in 1839. Credit for the first recognition of the association of brittleness of the bones and a blue appearance of the sclera is universally given to Eddowes,⁶ who in a brief note in the *British Medical Journal* in 1900 reported three

5. Bronson, E.: *Fragilitas Ossium*, *Edinburgh M. J.* 18:240 (April) 1917.

6. Eddowes, A.: *Dark Sclerotics and Fragilitas Ossium*, *Brit. M. J.* 2:222, 1900.

cases. I find, however, that the claim to priority by Spurway⁷ is justified. In the *British Medical Journal* in 1896, Spurway¹ described a family of fourteen persons in four generations; ten of these had had multiple fractures, and he noted that the only other abnormality common to many members of the family was a curious bluish tinge of the eyeball which in some members was very marked.

The publication of Spurway's findings apparently attracted little attention as the article has not been mentioned in any of the succeeding articles on the subject. In 1900 Eddowes in a short note called attention to the syndrome, and in 1908 Peters⁸ reported a family in which blue sclera was transmitted through four generations.

Since 1910 the syndrome has been widely studied, its hereditary nature has been established, and certain other conditions have been added to the original symptom complex of blue sclera and brittle bones. Chief among these is hereditary deafness, the occurrence of which was noted independently in 1917 by van der Hoeve and de Kleijn⁹ and by Bronson.⁵

3. REPORT OF CASE

History.—A girl, aged 12 years, was admitted complaining that her bones were easily broken, having had thirty-three fractures.

The father was living and well, and the father's family history was negative. The mother was living and in good general health. She had blue sclera, was deaf, and had had two fractures. The grandmother and the great-grandmother on the mother's side of the family had blue sclera and were deaf. It is not known whether or not they had fractures. The patient had three brothers and two sisters. All were living, and all had blue sclera. Two brothers and one sister had had multiple fractures.

The mother was a rather large woman, with a height of 66 inches (167.6 cm.) and weighing 184 pounds (83.5 Kg.). The maternal grandmother was of small stature.

The patient had been a normal full-term baby, had nursed six months, and had then fed on condensed milk. She began to walk at about 18 months. Her dentition was normal. In her second year she was severely ill with infantile diarrhea. There had been no illness since, except an occasional cold. She has had none of the exanthemas. Menstruation began at 12 years and was normal and regular.

Present Illness.—The first fracture occurred in her third year when she slipped and fell to the floor, breaking the right forearm. At the age of 3 she fell and broke her right leg. The leg was broken again the next year and healed in a position of deformity, and has not been straight since, though it was fractured several times manually, and at one time a wedge of bone was removed in an attempt to straighten it. She fractured the left femur once, both legs and both forearms

7. Spurway, J.: *Fragilitas Ossium, Blue Sclerotics and Otosclerosis*, Brit. M. J. 1:826, 1917.

8. Peters: *Blaufärbung des Augapfels*, Klin. Monatsbl. f. Augenh. 46:130, 1908; *Blaue Sclera und Knochenbrüchigkeit*, ibid. 51:524, 1913.

9. Van der Hoeve, J., and de Kleijn, A.: *Blauwe Sclera*, Nederl. Tijdschr. v. Geneesk. 1:1003 (March 31) 1917; *Blaue Sclera, Knochenbrüchigkeit und Schwerhörigkeit*, Arch. f. Ophth. 95:81, 1918.

several times, and both clavicles at least once. In all there had been thirty-three fractures. At the age of 6 she was given crutches and a brace for the right leg, but broke the left leg several times while wearing the brace on the right. During the period from 8 to 10 years she walked on her knees. During the last two years she had been confined to a wheel chair. The fractures had always occurred after very slight violence. The last one (the fracture of the right leg which at present was not united) occurred when she was walking on her knees, and attempted to get up on the curb. Her leg struck the curb and the bone was broken. The fracture occasioned so little pain that she continued to the theater where she was going and sat through and enjoyed the performance. Her father stated that this lack of pain had been a characteristic feature of all her fractures.

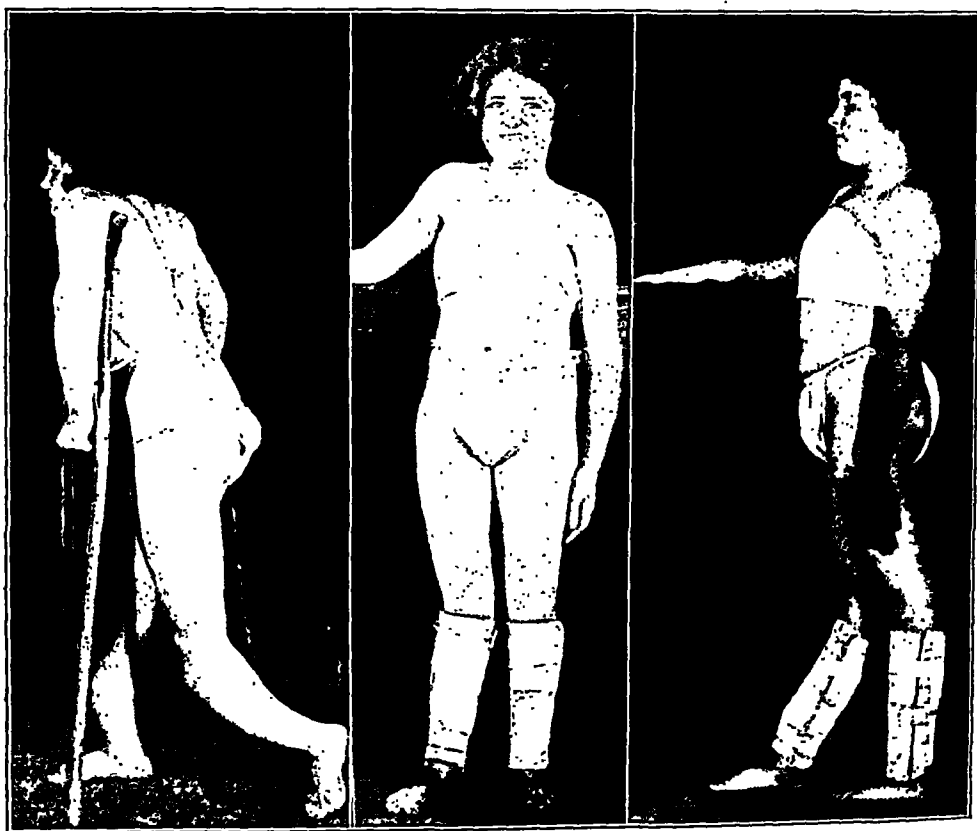


Fig. 1.—Patient with hereditary hypoplasia of the mesenchyme before and after correction of the deformities.

As an example he cited an instance when her physician was examining her left forearm eight weeks after a fracture: in testing for the firmness of union, the bone was heard to snap as it was broken again. But the patient "didn't bat an eye," and complained of little pain.

Physical Examination.—The patient was a rather obese young girl, with a height of 55.5 inches and weighing 101 pounds (45.8 Kg.). She was rather short and was unable to walk or stand without support (fig. 1). The skin was fair, rather dry and delicate in texture, and was covered with freckles. The hair of the head was abundant and brownish red. It was dry and coarse. The

eyebrows and eyelashes were normal. The axillary hair and pubic hair were normal. The nails were normal.

Head: The head was normal in contour, with a circumference of $19\frac{1}{2}$ inches (49.4 cm.). The ears were rather small. There was some retraction of the eardrums. The hearing was normal.

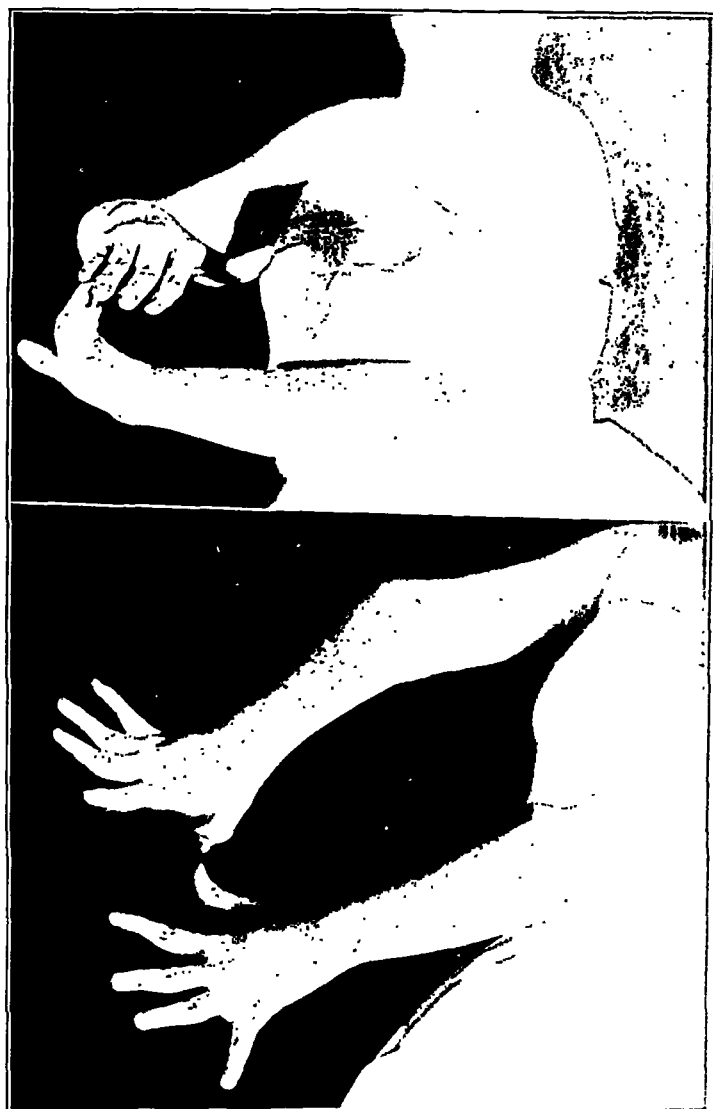


Fig. 2.—Passive and active hyperextension of the fingers, deformity of right elbow and freckles on arms.

Nose: The septum was slightly thickened, and both middle turbinates were slightly enlarged.

Eyes: The pupils were equal and regular. They reacted normally to light and accommodation. The ophthalmoscopic examination was negative. The extra-ocular movements were normal. Intra-ocular tension was normal. The sclera appeared to be a clear china blue in color. The blue tint was deeper in the

anterior part of the bulb in a zone around the cornea corresponding to the uvea. There was a slight embryotoxin.

Throat: The tonsils had been removed. There were some remnants of adenoid tissue present. The tongue was normal. The teeth were all present and in unusually good condition. They were normal in size and structure and in good alinement. There was one small cavity which was filled.

Glands: There was no glandular enlargement; the thyroid was not enlarged; the breasts were normal.

Chest: The chest was rather full and barrel shaped. The costal angle was about 90 degrees. Expansion was good and the lungs were normal.

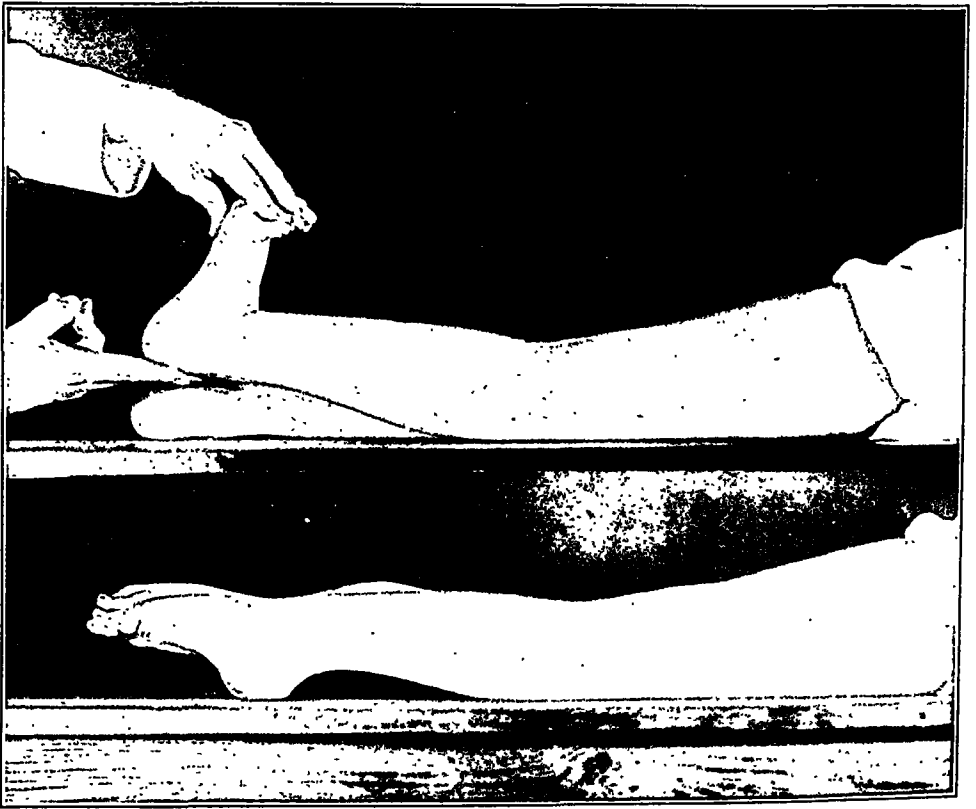


Fig. 3.—Hyperextension of the knee and range of motion in the ankles.

Heart: The heart was normal. The pulse was 80; the systolic blood pressure was 120, the diastolic 80. The arteries were soft. The abdomen was normal.

The external genitalia were normal. The musculature was normal except in the lower extremities, where there was some atrophy and weakness from disuse.

The reflexes were normal. Intelligence was normal. The spine was lordotic but otherwise normal.

Upper Extremities: The shoulders were normal. There were slight deformities of both elbows, the carrying angle being lost and the inner condyle of the humerus being higher than usual. Flexion of the elbows was normal. Extension was limited to 180 degrees on the right and 170 degrees on the left. Supination of the right forearm was limited. The fingers were slender and tapering. Movements of the wrists and fingers were more free than normal. It was possible to hyperextend the fingers to about 90 degrees (fig. 2).

Lower Extremities: The length of the right leg was 30 inches (76.2 cm.); of the left, 29¼ inches (74.2 cm.). The length of the right femur was 17 inches (42.5 cm.); of the left, 16¾ inches (42.4 cm.). The circumference of the right thigh was 16 inches (40.6 cm.); of the left, 15½ inches (38.7 cm.). The circumference of the right calf was 9¼ inches (23.4 cm.); of the left, 10¼ inches

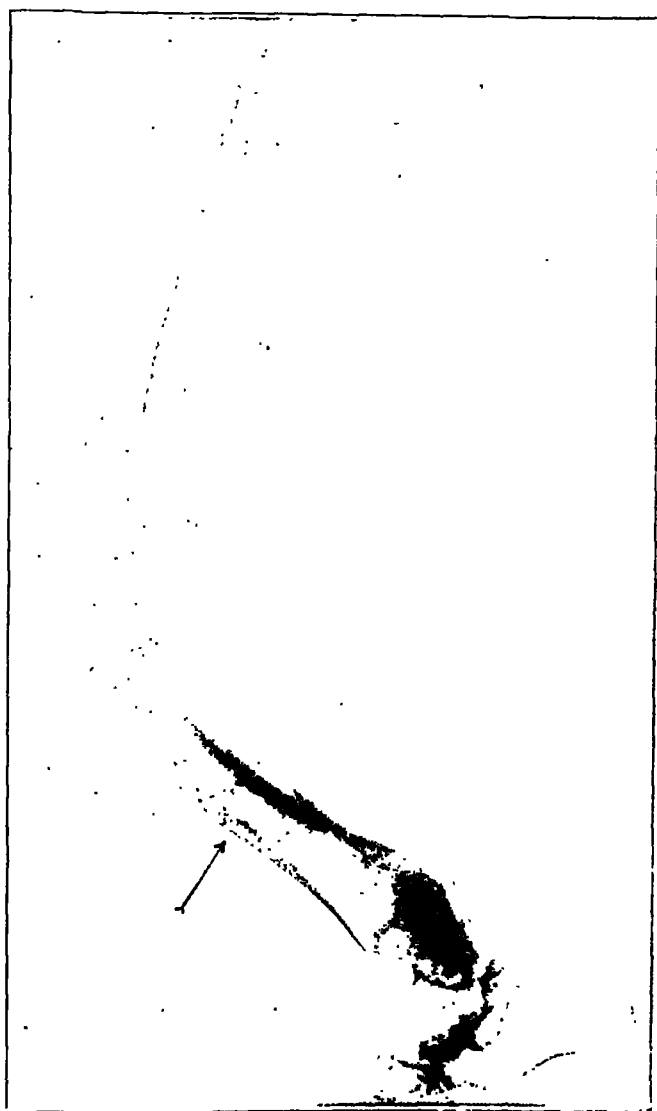


Fig. 4.—Sclerosis and deformity of the right tibia and fibula; the arrow points to a subperiosteal fracture due to a slight injury.

(26 cm.). The thighs were normal. The patellae were unusually small. There was a marked anterior bowing of the right leg; the apex of the curve was in the lower half of the leg and was covered by an extensive scar which was adherent to the bone. In this scar was a small ulcer. The curve described an arc of 70 degrees, and was chiefly in the lower half of the leg, the upper half of the leg being straight (fig. 4). On the left side there was an anterior bowing in the

upper third of the leg, the lower part of the leg being straight. The angle of the deformity was 60 degrees. There appeared to be an incompletely united fracture of the tibia at the apex of the deformity (fig. 5). The feet were relaxed and pronated. There was hypermotility of all the joints of the lower extremities (fig. 3).

Ankles: Flexion was to 50 degrees and extension to 150 degrees.

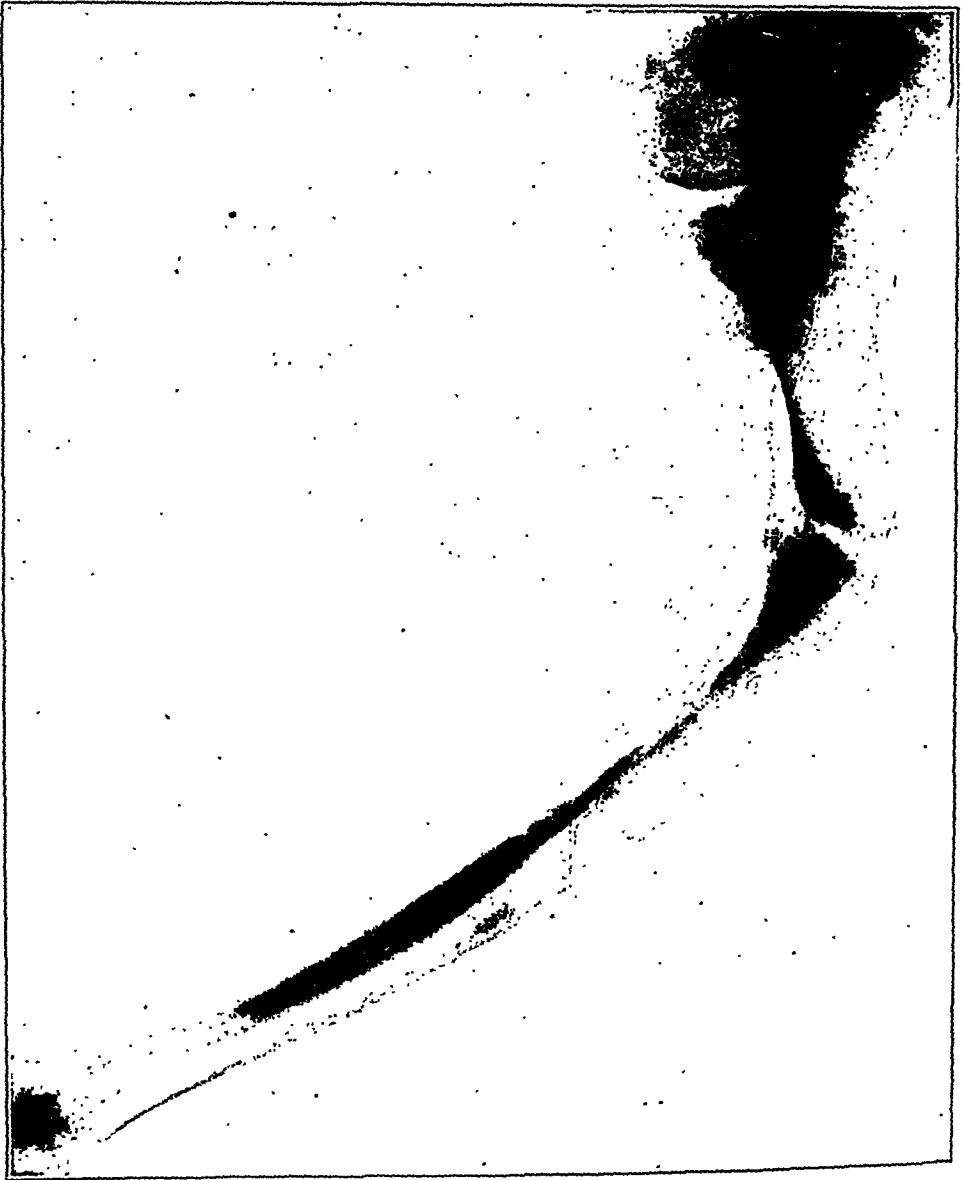


Fig. 5.—Sclerosis and nonunion of the left tibia.

Knees: There was increased lateral mobility and hyperextension on the right to 22 degrees, and on the left to 15 degrees. With the knee extended it was possible for the patient to flex the hip to such a degree that the heel could be placed over the shoulder and behind the head.

Urinalysis: The urine was consistently normal.

Blood: Hemoglobin was 85 per cent; red blood cells totaled 5,432,000; white blood cells, 10,500.

Differential Count: Polymorphonuclears totaled 51 per cent; polymorphonuclear eosinophils, 3 per cent; lymphocytes, 34 per cent, and monocytes, 12 per cent.

Basal Metabolism: The finding was —3, normal. The tuberculin, Wassermann and Schick tests were negative.

Blood Chemistry: The pH was 7.58; phosphates totaled 4.06 mg. per hundred cubic centimeters, and calcium, 12.17 mg. per hundred cubic centimeters.

The roentgenographic findings are given in section 11.

Operations.—An operation was performed on the left leg by Dr. G. C. Abbott, Jan. 5, 1925. An incision was made over the internal aspect of the junction of the upper and middle thirds of the tibia where there was a pronounced angulation forward. A pseudo-arthritis was found with massive sclerotic bone in the posterior half of the upper end of the lower fragment, and with a slight amount of sclerotic bone in the upper fragment. The bone was sectioned obliquely with removal of wedges from both fragments, one from the posterior aspect of the lower fragment and a second from the anterior end of the upper fragment. The fragments were then overlapped and fixed with two beef bone screws. It was not necessary to do an osteotomy of the fibula. A general anterior curvature of the tibia that could hardly be corrected remained, but the main deformity was greatly improved. The wound was closed with catgut to the periosteum, silk to skin. The leg was fixed in a plaster-of-paris cast. The step operation for the cure of the nonunion in the fracture of the upper third of the tibia is shown in figure 6.

February 15, convalescence was uneventful. The stitches were removed. The wound was clean.

February 18, the plaster was changed. Clinically the leg felt solid.

February 25, the patient while in a wheel chair struck her right leg against a bed. There was no swelling, ecchymosis or false motion, but there was slight tenderness over the lower third of the right tibia and the roentgen ray showed an incomplete fracture of the tibia at this point (fig. 4).

March 2, I performed an operation on the right leg. The rather extensive scar over the anterior surface of the apex of the curve in the tibia was excised by an elliptical incision about 5 inches (12.7 cm.) long. The scar was intimately bound to the periosteum, which was very thin and delicate, and was stripped from the bone with ease. The tibia was then exposed by stripping back the periosteum in the area of the curve, and with an osteotome a wedge with an anterior base was removed. The bone was very hard and brittle. The fibula was exposed through a lateral incision. In making this incision it was found that the fibula lay very deep in the leg and posterior to the tibia. There was a thick layer of superficial fat, and the fascia of the leg was not white and glistening as is normal but was a delicate pink connective tissue membrane. The fibula was divided with an osteotome. An attempt was made to correct the deformity, but shortening of the soft tissue on the posterior surface of the leg interfered with correction. A curved incision about 5 inches long was made on the posterolateral surface of the leg, and the tendon of achilles was exposed. The tendon of achilles was most unusual in that it was about the diameter of a lead pencil (one-fourth inch, or 0.6 cm.) and translucent in appearance, there being a striking absence of the dense white fibrous tissue usually seen. Its color was a delicate pink rather than white. The tendon of achilles was split longitudinally and sectioned by the Z method and lengthened about 2½ inches (6.2 cm.). The wound was then closed and an attempt was made to straighten the leg. There was

considerable difficulty in accomplishing this and the ends of the cut tibia were remodeled with the rongeur forceps so that the lower fragment was pointed on the upper end, and the lower end of the upper fragment hollowed out to form a socket into which the lower fragment fitted. It was then possible completely to correct the deformity; but, with this done it was found that the skin edges could



Fig. 6.—Left tibia eleven weeks after operation showing callus formation and beef bone screws in place.

not be made to close over the denuded bone. Consequently, a tension cut about 5 inches long was made through the skin on the lateral surface of the leg, and tension sutures of silk and catgut were used to draw the skin together. After this was placed, the tension sutures were removed. The tension incision was left open and covered with petrolatum gauze. The leg was encased in plaster with the deformity partly corrected.

In addition to the striking delicate pink color of the tendon of achilles and of the deep fascia as noted in this patient, there was an unusual friability of the soft tissues. The blood vessels tore easily. The periosteum was so delicate that it could be pulled apart with a pair of tissue forceps, and the scar over the tibia was much less dense than normal scar tissue. This condition of the fibrous

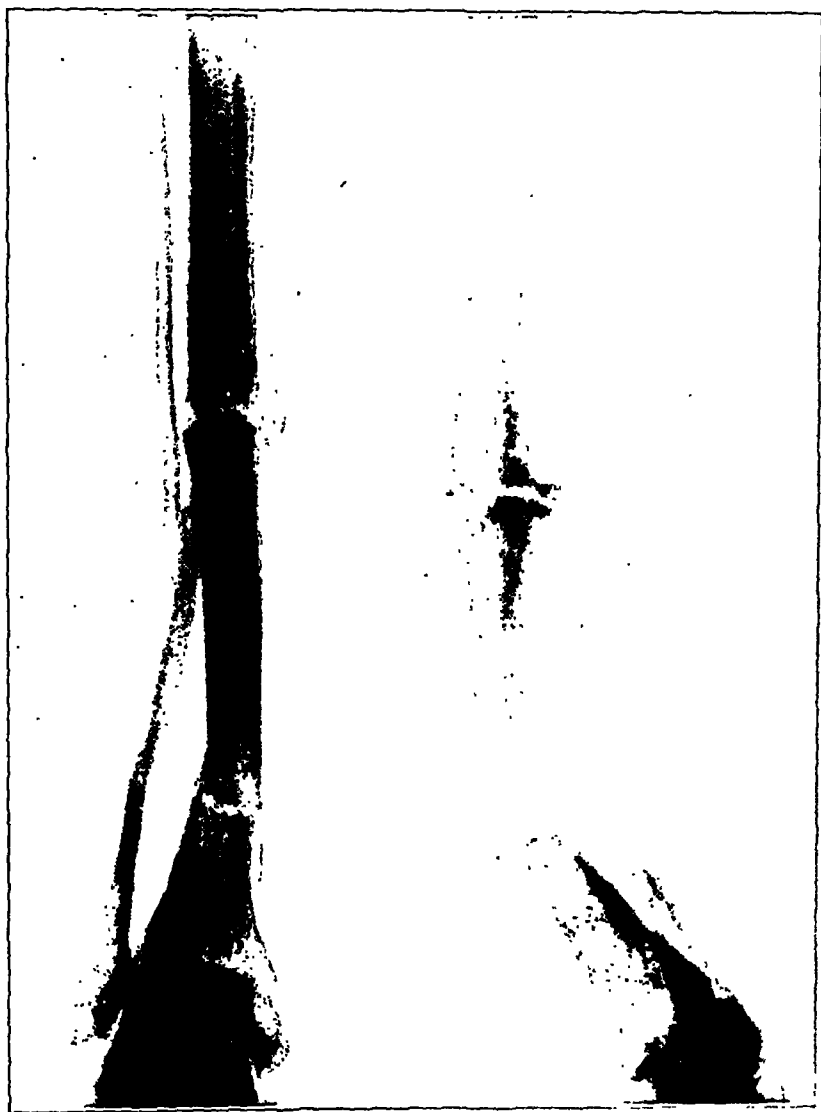


Fig. 7.—Right leg two weeks after osteotomy showing callus formation

tissue was in sharp contrast to that of the bone which seemed to be unusually hard and brittle.

March 12, the stitches were removed. The wounds were clean

April 2, the cast was changed. The union was firm. The deformity in the lower third of the leg below the site of the operation was still present

April 20, osteoclasis of the right leg was performed by Dr. Key. With the osteoclast the bone was fractured at the apex of the forward bow. The

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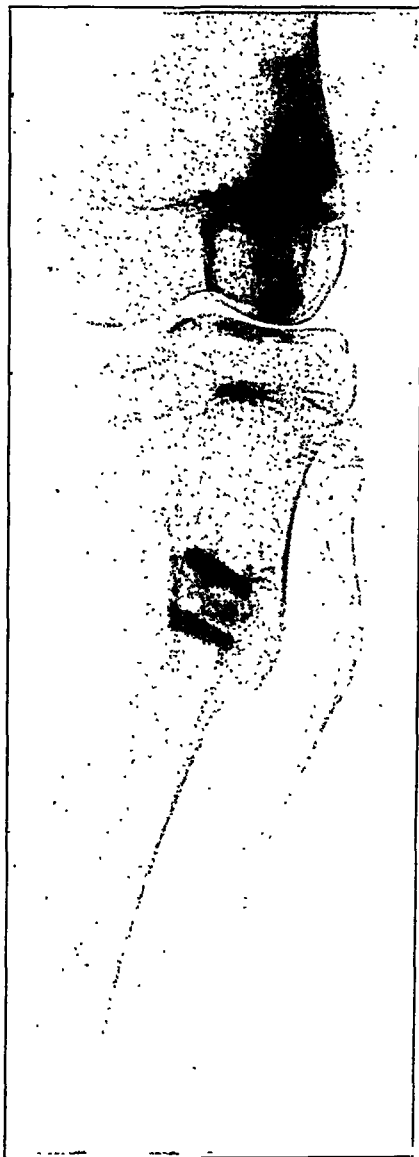


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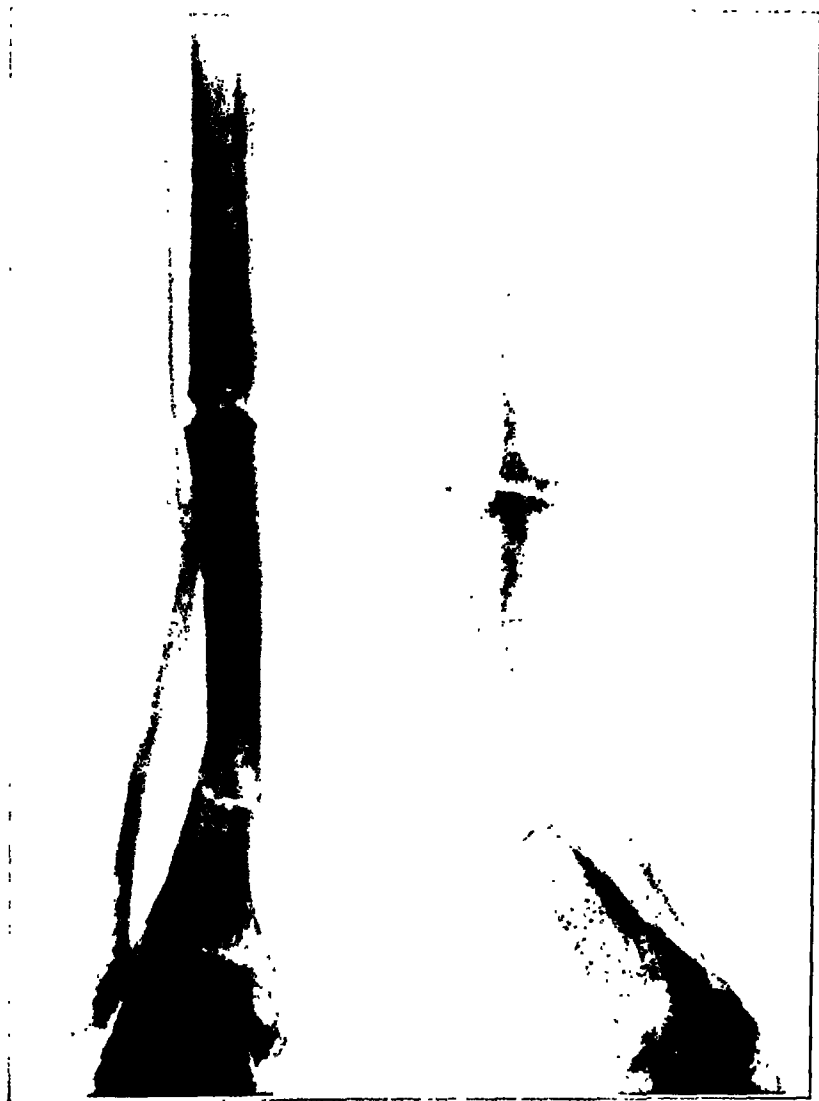


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bone was fractured with little force. The tender skin over the bone was lacerated by the pressure. This was dressed with picric acid and the leg was put up in plaster in the corrected position.

April 30, convalescence was uneventful; the abrasion was almost healed.

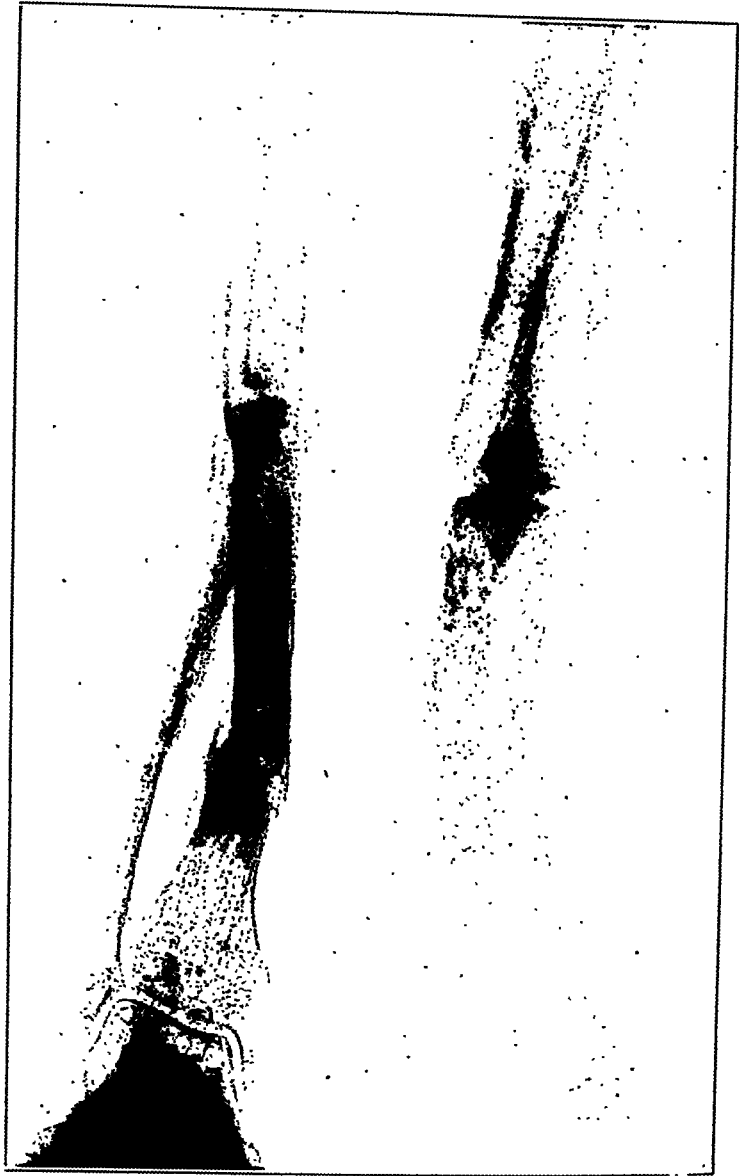


Fig. 8.—Right leg twelve weeks after osteotomy and eight weeks after osteoclasis below, showing callus formation and incomplete correction of the deformity.

May 20, the cast was changed. The union was firm. The deformity was not completely corrected, but on account of the marked genu recurvatum it was felt advisable not to correct fully the anterior bow of the lower leg (fig. 8).

June 10, the patient was learning to walk with short plasters around the legs (fig. 1).

June 30, the patient was discharged, walking with crutches, and was told to wear celluloid splints on the legs.

4. HEREDITY

It is to be emphasized that the factor of heredity is of fundamental importance in the condition with which we are dealing. Fragile bones or blue sclera occurring singly or together in a patient with no similar cases in the family cannot be considered as belonging to the group under discussion.

That the condition is hereditary was pointed out by Spurway¹ and Peters⁸ in their early articles.

During the last fifteen years many family trees have been published which show that blue sclera and brittle bones are dominant hereditary characteristics in certain families. The most important of these are sum-

Summary of the Reported Families with Hereditary Hypoplasia of the Mesenchyme

| Year | Author | Number | | Num-ber with Deaf-ness | Transmitted by | | Gen-erations | Affected | |
|-------------|---|--------------------|--------------------------|------------------------|----------------|---------|--------------|----------|----------|
| | | Num-ber in Fam-ily | of Sus-ceptible Per-sons | | Male | Fe-male | | Males | Fe-males |
| 1896 | Spurway ¹ | 14 | 13 | 10 | 10 | ? | 3 | 0 | 4 |
| 1908 | Peters ⁸ | 10 | 10 | 9 | 3 | ? | 2 | 2 | 1 |
| 1910 | Stephenson ¹⁵ and Harman ¹⁶ | 53 | 52 | 31 | 7 | ? | 1 | 10 | 5 |
| 1911 | Burrows ⁶ | 29 | 21 | 13 | 9 | ? | 1 | 4 | 4 |
| 1911 | Rolleston [†] | 6 | 6 | 4 | 1 | ? | 0 | 2 | 3 |
| 1912 | Adair-Dighton ³² | 12 | 12 | 9 | 5 | 1 | 2 | 1 | 1 |
| 1913 | Conlon ²⁵ | 27 | 22 | 18 | 6 | ? | 2 | 4 | 5 |
| 1914 | Cockayne ¹⁷ | 16 | 16 | 6 | 6 | ? | 0 | 3 | 4 |
| 1915 | Conrad and Davenport ¹² | 12 | 37 | 22 | 22 | ? | 1 | 5 | 4 |
| 1917 | Van der Hoeve and de Kleijn ⁹ | 22 | 17 | 10 | 10 | 11 | 0 | 3 | 4 |
| | | 6 | 6 | 6 | 5 | 3 | 2 | 0 | 3 |
| 1917 | Bronson ⁵ | 55 | 33 | 21 | 13 | 7 | 1 | 7 | 4 |
| | | 8 | 8 | 7 | 4 | 0 | 2 | 1 | 3 |
| 1919 | Hass ²⁰ | 24 | 14 | 8 | 8 | 7 | 2 | 2 | 3 |
| 1921 | Blegvad and Haxthausen ⁴¹ | 23 | 21 | 10 | 8 | 3 | 1 | 2 | 3 |
| 1921 | Freytag ³⁵ | 18 | 17 | 11 | 11 | 9 | 2 | 3 | 5 |
| 1922 | Alexander [†] | 6 | 6 | 6 | 4 | 1 | 0 | 3 | 4 |
| 1922 | Stewart [§] | 19 | 19 | 8 | 4 | 1 | 0 | 2 | 2 |
| 1923 | Straut ³⁴ | 10 | 10 | 6 | 5 | 3 | 0 | 2 | 3 |
| 1923 | Stoble ²⁴ | 66 | 39 | 18 | 8 | 8 | 4 | 4 | 5 |
| 1926 | Key..... | 9 | 9 | 7 | 4 | 3 | 0 | 3 | 3 |
| Totals..... | | 177 | 328 | 211 | 116 | 55 | 26 | 63 | 102 |

* Burrows, H.: Blue Sclerotics and Brittle Bones, Brit. M. J. 2:16, 1911.

† Rolleston, J. D.: Inherited Syphilis and Blue Sclerotics, Proc. Roy. Soc. Med. 4:125, 1910-1911; Ophthalmoscope 9:321, 1911.

‡ Alexander, J. B.: Fragilitas Ossium Associated with Blue Sclerotics in Four Generations, Brit. M. J. 1:677 (April 29) 1922.

§ Stewart, H.: Fragilitas Ossium Associated with Blue Sclerotics, Brit. M. J. 2:48 (Sept. 10) 1922.

marized in the accompanying table. The families of Voorhoeve¹⁰ and Bolten¹¹ are not included in the table because they are not typical.

The only study of the hereditary factor in fragility of bones which I found is that of Conrad and Davenport.¹² They were able to find thirty-five families in the literature in which two or more cases of fragile bones occurred. Only the last four families of the series belong to our

10. Voorhoeve, N.: Blue Sclerotics, Lancet 2:749, 1919.

11. Bolten, H.: Blaue Sclerae, Nederl. Tijdschr. v. Geneesk. 2:1747, 1923.

12. Conrad, H. S., and Davenport, C. B.: Hereditary Fragility of Bones, Eugenic Record Office Bull. 14, 1915, Cold Spring Harbor, N. Y.

group of blue sclera and brittle bones. They concluded that the factor that determines the imperfect, brittle development of the bones is a dominant one and that "a parent who is, or who was in early life, osteopsathyrotic will have half of his children so affected no matter whom he marries except that, if the consort be also osteopsathyrotic, it is to be expected that three-fourths of the children will be affected."

Unfortunately the authors did not distinguish between the three clinical types of *fragilitas ossium*. In their family 10 the second generation seems to have *osteogenesis imperfecta* and these children were all born of healthy parents. The others of the first thirty families seem to be cases of *osteopsathyrosis idiopathica*. In these the condition was transmitted by the father thirty-one times, and by the mother only four times.

In the cases of brittle bones and blue sclera the condition is more often transmitted by the mother to her children, though it may be transmitted by either the male or the female, and in certain families, such as Spurway's¹ and van der Hoeve's and de Kleijn's¹³ family Y, it was transmitted only by the male (table). In these families, there were no children born to affected females.

The characteristic feature of the heredity of blue sclera and brittle bones is that the condition is transmitted only by affected parents to their children. A generation is never skipped as is the case in hemophilia (knight's move of Bateson).

Children with normal sclera born of affected parents will have normal children. Furthermore, only the persons affected with blue sclera are subject to brittle bones and the other stigmas of the condition. The members with white sclera are also normal in other respects.

As was pointed out by Ruttin¹⁴ the fractures occur in childhood while the deafness comes on in adult life. That is one reason why so few cases of deafness are recorded in the accompanying table. The other reason is that it was not described as a part of the syndrome until 1917 and in most of the families reported deafness has not been looked for.

In the third column of the table is given the number of susceptible persons. A susceptible subject is a person one of whose parents was affected with the hereditary type of blue sclera. In the twenty-one families there were 388 susceptible persons. Of these 241, or 62 per cent, inherited the condition of hypoplasia of the mesenchyme.

In considering the incidence of multiple fractures the family of Stephenson and Harman will be omitted as the presence or absence of

13. De Kleijn (footnote 9, second reference).

14. Ruttin: Ohrbefund bei Osteopsathyrosis, *Monatschr. f. Ohrenh.* 54:305, 1919.

Scoliosis and kyphoscoliosis have been reported by van der Hoeve and de Kleijn⁹ and others. The small stature is in many cases partly the result of the deformities but in others it is simply due to the fact that the bones are shorter and slenderer than normal.

Bronson⁵ has called particular attention to the peculiar types of head found in the affected members of her two families. In the first family the frontal and occipital bones were unusually prominent yet there was none of the squareness of the rachitic head. The suture lines of the occipital bone were palpable and there was a history that two members of the family had had patent fontanelles throughout life. In the second family, the abnormality of the head was more pronounced. The characteristics of the head were "a frontal and supra-aural prominence; a slight tilting downward of the axis of the eye, ears bent outward and downward, and a slightly underhung jaw." This is a typical osteogenesis imperfecta type of skull.

In Ruttin's¹⁴ case the skull was of the hydrocephalic type and the sella was cuplike. Stenvers²³ noted an unusual configuration of the hind part of the skull. The deformity was a rather definite angulation of the occiput as though it had been folded on a hinge, and there was a clear fracture or vessel line in this region. This is similar to the occipital prominence noted by Bronson in the Currie family. In our case the head was rather large, 19½ inches (49.4 cm.) in circumference, and there was a definite prominence of the forehead, but there was no unusual occipital bulge or angulation (fig. 1). We do not consider the shape of the head as abnormal, and this is also true of six other affected members of the family of whom we procured photographs. Buxton, who examined the Oxford family reported by Stobie,²⁴ concluded that the heads were not abnormal.

6. THE EYES

An abnormal blue appearance of the sclera is an essential part of the clinical picture. As stated in the section on heredity, only those members of the family who have blue sclera are subject to the abnormalities to be described. The color has been described as a clear china blue, a slate blue or a gray blue. The depth of the blue varies in different individuals of the same family, as was noted by Spurway.¹ The color is not uniform but is darker in the anterior portion of the sclera over the ciliary body. Behind the ciliary body, which as a rule can be distinctly outlined on the sclera in these eyes, the lighter gray blue extends as far back as the sclera can be seen.

23. Stenvers, H. W.: Röntgenologische Bemerkungen, *Arch. f. Ophth.* 95:94, 1918.

24. Stobie, W.: The Association of Blue Sclerotics with Brittle Bones and Progressive Deafness, *Quart. J. Med.* 17:274 (April) 1924.

All authorities are agreed that the blue of the sclera is not due to a pigmentation but is the result of an abnormal transparency of the sclerotic coat of the eye which permits the blue uvea to shine through. Eddowes⁶ suggested that the transparency of the sclerotics indicated a want of quantity or quality of the fibrous tissue forming the framework of the various organs of the body and probably explained the want of spring or toughness in the bones of these persons.

Peters⁸ believed the sclera to be actually thinner than normal. Conlon²⁵ was able to demonstrate the increased transparency by means of a Sach's lamp. He considered the unusual transparency as probably due to some change in the quality of the tissue rather than to an actual thinning of the sclera. In support of this view he stated that if the sclera were thinned one would expect to find cases of buphthalmos in these families, or at least of axial myopia.

Fridenberg, who examined Herrman's²⁶ case, stated that if the sclera were thin, some cases should show distention of the globe, as in infantile glaucoma or hydrophthalmos or coloboma or posterior staphyloma. He suggests that the blue sclerotic and lead gray iris are due to a transparency dependent on the absence of lime salts in the connective tissue of the sclera and iris.

In the two instances in which blue sclera were subjected to histologic examination exactly opposite conclusions were drawn. Buchanan²⁷ studied an eye removed from a girl aged 9 years who had blue sclera. The removal was necessitated by an injury to the eye. In this eye the cornea was three-fifths and the sclera was only one-third the normal thickness. There was a decrease in the number but no change in the size of the sclerotic fibers.

Bronson⁵ reported the condition of the sclera of an infant aged 11 months who was a member of her first family and who had blue sclera. The eye was removed post mortem. J. V. Patterson examined the sections and stated that the sclera was of normal thickness and that the size and number of the fibers were normal for a child of that age. Bronson stated that Buchanan's case had no family history of fractures and that one has no reason to assume that it belongs to the fragilitas blue sclerotic group.

Embryotoxon was noted by Peters⁸ in the family described by him. It is apparently not of great significance in the syndrome. It was present in the families reported by Stephenson,¹⁵ Harman,¹⁶ Conlon,²⁵

25. Conlon, F. A.: Five Generations of Blue Sclerotics and Associated Osteoporosis, Boston M. & S. J. **169**:16, 1913.

26. Herrman, C.: Blue Sclerotics and Brittle Bones, Am. J. Dis. Child. **9**:203 (March) 1915.

27. Buchanan: A Case of Maldevelopment of the Cornea and Sclerotic, Tr. Ophth. Soc. **23**:267, 1903; Ophthalmoscope **8**:685, 1910.

and in the family Y of van der Hoeve and de Kleijn⁹ but was absent in their family X. A slight embryotoxon was present in our case. Keratoconus was present in Behr's²⁸ case. Stephenson noted a Fuch's coloboma in his case. Cataract was present in two of the cases of van der Hoeve and de Kleijn. Most of the cases that were refracted showed astigmatism and hypermetropia (Conlon, Stephenson, Harmon, Bronson, van der Hoeve and de Kleijn and others). Myopia was noted five times by van der Hoeve but was not present in the other families described. The fundi were uniformly negative in all cases examined. The intraocular tension was normal.

It is to be noted that blue sclera occurs in other conditions, such as congenital buphthalmos, and when the whole development of the eye is backward. It may occur apparently spontaneously in persons normal in other respects, as in Bronson's Mrs. L. A slight blueness of the sclera may be present in anemia, tuberculosis and certain forms of heart disease.

On the other hand, there are a number of cases in the literature in which blue sclera and fragile bones occurred sporadically in persons in whose families there had been no similar cases: Bronson,⁵ Herrman²⁹ Ostheimer,²⁹ Hoffmann,³⁰ Gutzeit³¹ and others. Whether or not these cases belong in the group under discussion it is impossible to say. They certainly resemble our case in a great many ways. However, I have found no record to the effect that the disease has been transmitted to children in such a sporadic case.

7. DEAFNESS

The first mention of deafness in a case of mesenchyme hypoplasia was in 1912 by Adair-Dighton,³² who simply noted its presence in a member of his family. Likewise Behr²⁸ in 1913 noted deafness in his case. The credit for definitely including hereditary deafness in the syndrome should be divided between van der Hoeve and de Kleijn⁹ and Bronson,⁵ who described the condition almost simultaneously in 1917.

Van der Hoeve and de Kleijn reported two families. In the first family all of the eleven patients with blue sclera who were examined were deaf. The deafness was of the otosclerotic type in all cases, but

28. Behr, C.: Beitrage zur Aetiologie des Keratoconus, *Klin. Monatsbl. f. Augenh.* **51**:281, 1913.

29. Ostheimer, M.: Fragilitas Ossium, *J. A. M. A.* **63**:1996, 1914.

30. Hoffmann, W.: Ueber Blaufärbung der Sklera und abnorme Knochenbrüchigkeit, *Arch. f. klin. Chir.* **107**:279, 1915.

31. Gutzeit, R.: Ueber blaue Sklera und Knochenbrüchigkeit, *Klin. Monatsbl. f. Augenh.* **68**:171, 1922.

32. Adair-Dighton, C. A.: Four Generations of Blue Sclerotics, *Ophthalmoscope* **10**:188, 1912.

in the advanced cases this was complicated by labyrinthine disease (nerve deafness). In the second family three of the six affected persons were deaf. They emphasize the fact that in many of the younger patients the beginning deafness had not been noticed but was brought out by the aural examination.

In Bronson's Currie family there were eight adults who had blue sclera and seven of these developed deafness in early adult life. The other adult died at the age of 23 and deafness had not been noted. Three of her patients were examined by J. S. Frazer. All showed otosclerosis and one also had nerve deafness. One adult of this family who had white sclera was examined and found to have normal hearing.

Four of Voorhoeve's¹⁰ patients were examined for deafness and all showed labyrinthine deafness. Ruttin¹⁴ gave a detailed examination of the deafness in his case and noted that the deafness develops in later life while the fractures occur in early life. Hass,²⁰ Straat,³³ Freytag,³⁴ Blenke²¹ and Weichmann and Pool¹⁹ noted deafness in varying degrees in their families. In the family of our patient the mother is deaf and so was the maternal grandmother. The family is widely scattered and it has not been possible to examine these or to get a detailed history of the other adult members of the family. Our patient is now 12 years old and her hearing is apparently normal, but it is probable that she will develop deafness in adult life.

To explain the deafness in her cases, Bronson assumes that there was a deposit of calcium salts in the middle ear. Stenvers,²³ in studying the skulls of the families of van der Hoeve and de Kleijn roentgenographically, found that the petrous bone cast a dense shadow and that there was a compact opaque mass covering and obscuring the entire vestibular region. From these findings he was able to make a clinical diagnosis of sclerosis and abnormal calcification of the labyrinthine system. Ruttin confirmed the presence of otosclerosis by histologic examination of the petrous bone.

8. FRACTURES

Multiple fractures are a characteristic feature of any series of cases of hereditary hypoplasia of the mesenchyme, though they are by no means present in every person affected with the blue sclera. In the 210 persons in the accompanying table who had blue sclera 146 had multiple fractures, an incidence of 70 per cent. It is to be emphasized that if one of the parents has blue sclera the children are liable to have brittle bones even though the parent had no fractures. The incidence of frac-

33. Straat, H. L.: *Blauwe Sclerae, Fragilitas Ossium en Otoklerose*, Nederl. Tijdschr. v. Geneesk. 1:152 (Jan. 13) 1923.

34. Freytag: *Ueber blaue Sklera u. Knochenbrüchigkeit*, Klin. Monatsbl. f. Augenh. 66:507, 1921.

tures in the children of parents with blue sclera is 42 per cent (table). In our family the mother has blue sclera but has had no broken bones. Four of the six children have had multiple fractures. The other two children are still quite young.

In contrast to osteogenesis imperfecta the fractures are not as a rule present at birth and are not spontaneous. In most cases they occur in early childhood and are always assignable to a definite cause, though the causative force is often less than would be necessary to break a normal bone. The fractures continue to occur off and on through childhood. In most instances the tendency of the bones to break easily decreases after puberty, and the average patient, if not crippled by deformities due to malunion of fractures received in childhood, is able to pursue a normal life. However, sometimes the brittleness of the bones persists into late adult life.

The number of fractures is not as a rule great. The average patient probably suffers from six to eight fractures, and it is unusual for any of these unfortunates to have more than ten. Our case with thirty-five fractures in a period of ten years is, with the exception of the case with sixty-one fractures reported by Terry,³⁵ the most severe that I have seen recorded. This is in sharp contrast to osteogenesis imperfecta, in which great numbers of fractures are the rule. Many of these children pass through a period of from one to two years when fractures are very frequent. In our case this period included the eighth and ninth years of life. During this time the patient hardly recovered from one injury before another occurred.

The long bones, especially those of the lower extremities, are the ones most frequently affected. In our case there were fractures of both clavicles, both arms, both forearms, one thigh and both legs. In the literature are instances of fractures of the mandible, ribs, patella, pelvis and fingers. The bones of the face, the scapula, the sternum and metacarpals, and the bones of the ankle and foot seem not to have suffered. There are no definite instances of fracture of the spine or skull, though the roentgenograms of Stenvers²³ are suggestive of old fractures in all of these regions.

In some cases certain bones seem to be especially brittle. European observers feel that the femur is fractured more frequently than any other bone. In our case the femur was broken only once, and the majority of the fractures occurred in the legs. Conard and Davenport¹² believe that the tendency to fracture certain bones is inherited, the weak bones varying in different families. The reports in the literature are too cursory to permit a checking up of this theory at present.

35. Terry, W. I.: Hereditary Osteopsathyrosis, *Ann. Surg.* 68:231 (Aug.) 1918.

In regard to the character of the fractures, they are usually simple transverse or oblique breaks. Some of them are subperiosteal without displacement. Others are incomplete, being simply cracks in the bone (fig. 5). Greenstick fractures apparently do not occur and I know of no instance in which one of these fractures was comminuted. There is a history of a compound fracture of the right tibia in our case. It is the only one in the literature, I believe.

Reye³⁶ found most of the fractures occurring in the shafts of the long bones at the ends of the diaphysis near the epiphysis. In the other cases in the literature and in our family they have been limited to the diaphysis, but no particular region of the diaphysis has been favored. In this connection it is remarkable that there is no instance of a fracture of the neck of the femur in any of these families. The shafts of the bones are apparently so much weaker than the epiphyses that epiphyseal fractures do not occur. Likewise, there are no instances of epiphyseal separation among these cases.

The amount of pain and swelling occasioned by a fracture seems to vary in different cases. In our case they were relatively slight. This is contrary to the experience of Hass²⁰ and Blencke,²¹ both of whom found a degree of pain in their cases commensurate with the fracture. The pain was, however, relieved by rest of the extremity. It is probable that the pain and damage to the soft parts vary inversely with the force exerted in producing the fracture. Their cases had relatively few fractures; our case had a great many. Any one who has seen acute fractures from slight violence to atrophic bones must have noticed that the pain and swelling are much less than occur in similar fractures caused by severe trauma to normal bones. In our patient the fractures were usually the result of slight force and were consequently accompanied by little damage to the soft parts and were not very painful.

Rapid healing of the fractures was noted by Spurway¹ in the first family reported. He stated that in one instance consolidation was quite firm at the end of four days. Hass²⁰ and Singer¹⁹ report fairly firm union in from four to eight days. We discovered this to our chagrin in the treatment of our case. In the correction of the long curve in the right leg, the osteotomy corrected the upper part of the curve. The lower part was to have been corrected by an osteoclasis but the injury to the very tender skin necessitated a window in the cast for dressings. A forward bowing of the tibia occurred under the window and almost reproduced the original deformity. Twelve days after the operation we attempted to remold the limb manually, but the union was so firm that we were unable to do so. When the patient began to walk the marked

36. Reye: Ueber diffuse Blaufärbung der Sklera, *Deutsche med. Wochenschr.* 4:125, 1917.

genu recurvatum caused us to leave the slight anterior bow in the lower leg as her line of weight bearing seemed to be better than it would be if the bone were straightened.

The fractures tend to heal with a minimum amount of callus and deformity. This, I believe, is due to the fact that in many of the fractures there is little or no displacement and a minimum amount of damage to the soft parts and stripping up of the periosteum. In our case postoperative roentgen-ray examination showed about the normal amount of callus (figs. 6, 7 and 8). The nonunion of the left tibia in our case is, I believe, the only case of nonunion in this condition which has been reported (fig. 5). It was probably the result of inefficient fixation as the bone united promptly after operation. The nonunion of the patella reported by Gutzeit³¹ occurred in a nonhereditary case.

Hass²⁰ noted that so firm is the union that refracture through the seat of an old fracture practically never occurs. This is probably true because the healing of a fracture in these cases is often accompanied by more or less sclerosis of the bone. In many instances the fractures heal perfectly and leave no sign even in the roentgenogram. However, in our case, in spite of the marked thickening of the cortex of the right tibia, it has been broken ten or twelve times in the lower half of the shaft (fig. 4).

9. DEFORMITIES

Many of these patients develop severe crippling deformities, especially of the lower extremities and spine. It is to be emphasized that these deformities are the result of malunion of fractures and are preventable. That they are not due to softening of the bones is illustrated by the necks of the femora and the contour of the pelvis in our case. Were the bones softened one would expect to find an osteomalacic type of pelvis and a bilateral coxa vara. On the contrary, the pelvis is normal in contour and there is a definite bilateral coxa valga (fig. 9). The coxa valga is probably a secondary change in the angle of the neck of the femur due to the fact that in this patient weight bearing has been considerably restricted since infancy. As will be mentioned below, the bones are unusually hard but brittle.

In our case, the shafts of the femora though slender are normal in contour. The deformities of the legs are clearly the result of old fractures. There is even less secondary curving in the bone above and below the deformity than one usually finds in such cases in growing children (figs. 4 and 5). The deformities of the forearms, elbows and clavicles are clearly the result of old fractures. The bones that have not been broken, though slender, are not bowed.

Scoliosis and kyphosis have been reported in several instances. Stenvers²³ noted that in those cases with kyphosis and scoliosis the deformities were sharp and angular such as result from mild crushing

fractures of one or more vertebral bodies rather than gradual curves, such as one would expect to find if the deformities were the result of general bone softening. Another possible explanation of these spinal curves is that they are due to the general laxity of the ligaments of the body. In our case the spine was lordotic and unusually flexible for such a short and heavy torso.

10. CONDITIONS OF THE JOINTS AND MUSCLES

In those affected with hypoplasia of the mesenchyme the fibrous structures supporting the joints are unusually loose, and the range of motion in the joints is greater than is found in the average normal person of a similar age and physical type. This laxity of the ligaments in some families leads to frequent sprains and dislocations. In the first description of the condition Spurway¹ stated that the members of his unfortunate family suffered from bruises and sprains without number. One member of the family suffered a dislocation of the elbow.

Conlon²⁵ reported a dislocation of the hip associated with a fracture of the femur in a girl, aged 12, who was a member of his family. The injury resulted from a fall of only a few inches, but he laid no stress on the occurrence of a dislocation in this family. Behr³³ in 1913 first emphasized the fact that the joints in these cases are often abnormal. His patient was a small undernourished woman, aged 38, who had had dislocations of the foot, knee, right shoulder and recurrent dislocation of the left shoulder. The family history was not given but the fact that the patient developed otosclerosis at 19 years leads us to include her in the hereditary group. As the roentgenograms of the joints showed no abnormality of the bone, Behr concluded that the joint capsules were at fault and that the condition was a congenital defect due to a disturbance of the internal secretions.

In the Currie family reported by Bronson⁵ dislocations were almost as frequent as fractures, and occurred only in those members who had blue sclerotics and brittle bones. This observation of Bronson's to the effect that dislocations are almost as frequent as fractures has not been borne out by other observers, as few instances are recorded in the literature. Freytag³⁴ reported a case in which the patient had dislocation of the patella at 2 years of age. In one of Singer's¹³ patients a dislocation of the clavicle occurred at 5½ years, and one dislocation of the shoulder occurred in a member of the second family reported by van der Hoeve and de Kleijn.⁹ From these meager reports one would judge that dislocations are rather rare among these cases.

Sprains are perhaps slightly more common than are dislocations. They were first noted by Spurway,¹ and Cockayne¹⁷ from the large number of sprains which occurred in the family studied by him concluded that the ligaments were abnormally weak and that there was

Several other authors have mentioned and illustrated the roentgenograms of certain bones. Conlon²⁵ stated that in his case the long bones presented a thin cortex and a broadened medullary canal. On the shaft of the femur were irregular enlargements over which the cortex was very thin. The epiphyses were much broadened and devoid of a cortical outline.

Cockayne¹⁷ noted that in his family the long bones that showed no evidence of fracture exhibited no trace of rickets and were normal except near the ends where they were more transparent than normal. Somewhat similar findings were recorded by Reye³³ whose case showed high grade atrophy affecting only certain bones, and the atrophy was most pronounced near the ends of the diaphysis where the fractures usually occurred. Bronson⁵ did not describe the roentgenograms of the bones in any of her cases but some of her illustrations show rarefaction of the bones.

Voorhoeve¹⁰ described a very thin cortex which stood out sharply from the surrounding tissues. The bones contained only a slight proportion of lime salts and showed a rarefaction of trabeculae. In certain fractures little or no endosteal but very strong periosteal callus had been formed. A somewhat similar picture was present in the case reported by Hass.³⁰ The long bones were very short with a broad marrow cavity and a thin cortex (excentric atrophy). The epiphyses were normal in contour but small and surrounded by a thin shell of compacta. The trabeculae of the epiphyses were decreased in number.

In Singer's¹⁸ case there was a diffuse atrophy of the entire skeleton, with bending of some of the long bones. The only sign of the previous fractures was a sclerosis of the middle third of the left tibia. The skull was unusually long. The base was normal but the vertex was very thin and appeared to be composed of several islands of bone surrounded by dentate suture lines. The inner table was only 1 mm. thick. In the case of Weichmann and Pool¹⁹ the upper third of the shaft of the femur was thin and bowed. The carpal bones were rarefied and the bones of the hand were very thin.

We have roentgenograms of the entire skeleton of our patient. The skull is normal in contour and there is no evidence of old fractures. The bones of the skull and face are thin and less dense than normal. The paranasal sinuses and mastoid cells are well developed. There is no abnormal sclerosis of the petrous portion of the temporal bone. In the vertex the suture lines are rather faint and the region of the lambdoid suture is occupied by a number of unusually large wormian bones which are similar to the bone islets present in Singer's case. The external table is thin over the occiput. The sella is normal. The teeth are normal.

The spine shows no scoliosis or kyphosis. The bodies of the vertebra are definitely smaller than is normal for a person of 12 years. They are of about the normal density and are of the heavy type (broad and short). The laminae and spinous processes are normal and no spina bifida is present. In the lumbar region the transverse processes are small and short (fig. 9).

The ribs are of normal density but unusually slender, especially in the region of the posterior angle. The upper five ribs abruptly sag



Fig. 9.—Pelvis: normal contour, coarseness of bone structure and bilateral coxa valga should be noted.

downward and inward from the posterior angle. The bone structure of the ribs is coarsened.

The clavicles are slender and have a thick dense cortex and a narrow central canal. In each there is evidence of an old fracture of the middle third. At this point the cortex is thickened and there is a break in the line of the bone. The scapulae are normal.

The shafts of the humeri are slender while the epiphyses are of about the normal size. In the shaft the cortex is relatively thickened and the marrow cavity is reduced in diameter. The bone structure is

coarsened, especially in the lower portion of the diaphysis where the large trabeculae are clearly visible. There is no evidence of the old fractures (fig. 10).

In the region of the elbow the epiphyses are all united and the bone is of normal density. The coronoid processes are unusually large.

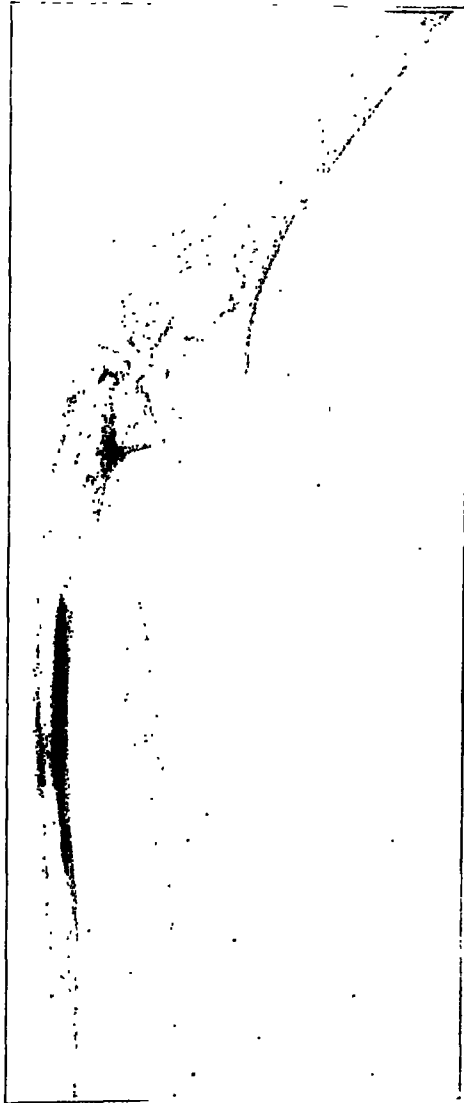


Fig. 10.—Right elbow: deformity and concentric atrophy of the long bones should be noted; the striation of the thick cortex is faintly visible.

There is a gentle posterior bowing of the shafts of the ulnae, which is more marked on the right side. With the forearm pronated the head of the radius projects one-fourth inch (0.6 cm.) beyond the external condyle. The shafts of the bones of the forearms are slightly less in

diameter than is normal and have a thick cortex and a narrow marrow cavity. In structure the cortex is faintly striated; the striations run parallel with the long axis of the bone. The lower ends of the bones of the forearm and the carpal bones are normal. The metacarpals and phalanges are rather slender and the cortical bone presents the longitudinal striations mentioned above (fig. 11).

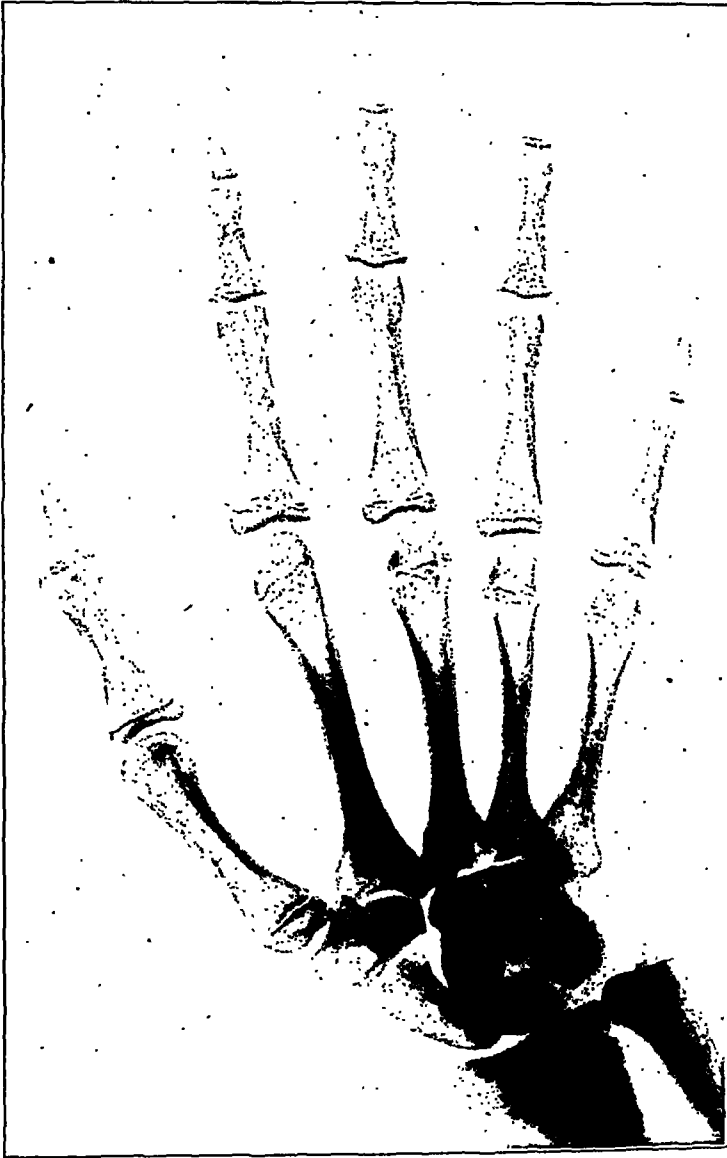


Fig. 11.—Right hand: the bones are slender and the structure coarsened.

The pelvis is broad and symmetrical and of the normal female type. There is no evidence of any fractures or of deformity due to softening of the bones. The sacrum is set unusually high as though it had slipped upward about one-fourth inch. The pubic rami are rather

slender. The bones are definitely more radiant than normal and the trabeculae are larger and fewer in number than normal. In the region of the sacro-iliac joints the bone is coarsely granular in appearance (fig. 9).

The two femora are similar in size and contour. The femoral head is rather small (diameter, $1\frac{11}{16}$ inches on the plate), and faces directly upward, the epiphyseal line being approximately horizontal. The neck is rather narrow (diameter, 1 inch), and is in a valgus position (collodiaphyseal angle, right 165 degrees and left 150 degrees). The great trochanter is large and is not yet united. The lesser trochanter is united to the shaft. The diaphysis is slender (diameter, three-fourths inch), and the marrow cavity is narrow (one-quarter inch diameter), occupying only about one third of the width of the bone. The lower end of the femur is approximately normal. There is a slight genu varum (fig. 6). The density of the bone is perhaps slightly less than normal and the bone structure of the cancellous bone is coarser than normal. The patella is small.

The leg bones have been fractured frequently and present different deformities. In the upper third of the left tibia there is a fracture that is not united. The fibula is united. In the region of the fracture there is an anterior bowing of 60 degrees. The shaft of the tibia is rather slender and the cortex is thin, especially on the anterior convex surface. In the region of the fracture the bone ends are unusually dense and the marrow cavity is obliterated by sclerotic bone. The bones are less dense than normal and the cortex is striated (fig. 5).

In the right leg the bones are bowed anteriorly 70 degrees, the deformity being a long curve in the lower half of the leg. The fibula is thin except in the region of the deformity, where it is thickened. The tibia is rather slender but is definitely denser than that of the left leg. The cortex is thickened anteriorly in the upper half and posteriorly on the concave side of the curve in the lower half. In the region of the deformity the bone is sclerotic and the narrow marrow cavity is crossed by frequent trabeculae. The cortex is striated. The epiphyses of the leg bones are decreased in density but normal in other respects (fig. 4).

The bones of the feet are markedly decreased in density and the shafts of the metacarpals and phalanges are very slender. While our patient was under observation we studied roentgenographically the healing of the operated bones and of the incomplete fracture in the tibia.

In the incomplete fracture (fig. 4) the bone united with no visible callus; the ends simply grew together and the fracture line disappeared.

In the fracture caused by the osteoclast there was a small amount of periosteal callus formed on the mesial and lateral aspect of both fragments (fig. 8).

The osteotomy of the tibia seemed to grow together also with a minimum of callus when viewed from the lateral aspect, but on antero-posterior view disclosed fairly extensive periosteal callus on both sides of the fracture. Endosteal callus also seemed to be definitely present. The separated ends of the fibula united by a massive callus (figs. 7 and 8).

In the left tibia where the bone ends were reshaped and screwed together a fairly extensive callus was quickly formed. It extended around the bones and filled the space between them. The fibula in this case threw out an extensive periosteal callus on the inner side of the fracture (fig. 6).

In our patient the bones of the skull and face are thinner than normal. The short bones are about normal though perhaps a little decreased in size, and the long bones have epiphyses that are approximately normal, but the diaphyses all show definite concentric atrophy. The density of the bones is about normal for bones of the same size, except in the lower extremities where the bones are decreased in density. This lack of the normal amount of mineral matter in the leg bones is probably an atrophy of disuse, as our patient had not walked for about three years. An unusually coarse structure of the cancellous bone was noted in our case. There was also an abnormal striation of the cortex of some of the long bones.

It is to be noted that the bones described in the literature fall into two groups: eccentric atrophy with a thin cortex and a wide marrow cavity, and concentric atrophy with a rather thick cortex and a narrow marrow cavity resulting in an unusually slender diaphysis. At present it is not possible to say whether or not either type is characteristic of a given family, or which type is the more common.

12. PATHOLOGY

Other than the descriptions of the sclerae referred to above, the pathology of the tissues in the hereditary hypoplasia of the mesenchyme is not in the literature. From the two operations performed on our patient we obtained specimens of the bone, the skin and scar tissue, the tendon of achilles and striated muscle.

Gross Examination of Bone.—The surface of the tibia is less smooth than normal. The periosteum is adherent but friable and when pulled off small bits remain attached to the bone. The cortex is unusually thick and very hard. The brittleness was evident when in attempting to cut a fragment with a sharp chisel the bone was broken rather than cut. On section the cortical bone appeared to be unusually

porous, being perforated with numerous canals easily visible to the eye. No typical cancellous bone was obtained.

Microscopic Examination.—A small piece of bone was cut in thin cross and longitudinal sections with a jeweler's saw. The sections of the dried bone were then ground on a hone until they were very thin. They were then dried and mounted in balsam. The rest of the tissue was fixed in Zenker's fluid. The bone was decalcified in hydrochloric acid in 95 per cent alcohol solution. Small pieces left in Muller's



Fig. 12.—Cortex of right tibia (cross section): the numerous wide canals containing a very vascular connective tissue should be noted (32 mm. objective).

fluid were not decalcified after three months. The tissue was embedded in paraffin or celloidin and sections were stained by a variety of methods. All sections examined showed an unusually thick cortex which was penetrated by a great number of wide canals and resembled embryonic bone. In the main these canals ran parallel to the long axis of the bone but by means of large transverse and oblique branches they communicated freely with one another, with the marrow cavity and with the periosteal surface—Volkmann's canals (figs. 12 and 13). The

cross and oblique canals are so numerous that it is often difficult to determine whether a given section is a cross or a long section of the bone. In the dense bone between the larger canals a few typical haversian canals are present. These, too, run irregularly through the bone and in some instances can be seen to communicate with the large canals. In some areas large dense masses of bone are seen in which no canals are present.

The wide canals contain a delicate myxoma-like connective tissue (figs. 14 and 15). This tissue is very vascular and in some of the larger canals twenty or more vessels may be present. The larger vessels run roughly parallel to the axis of the canals but some of the smaller vessels

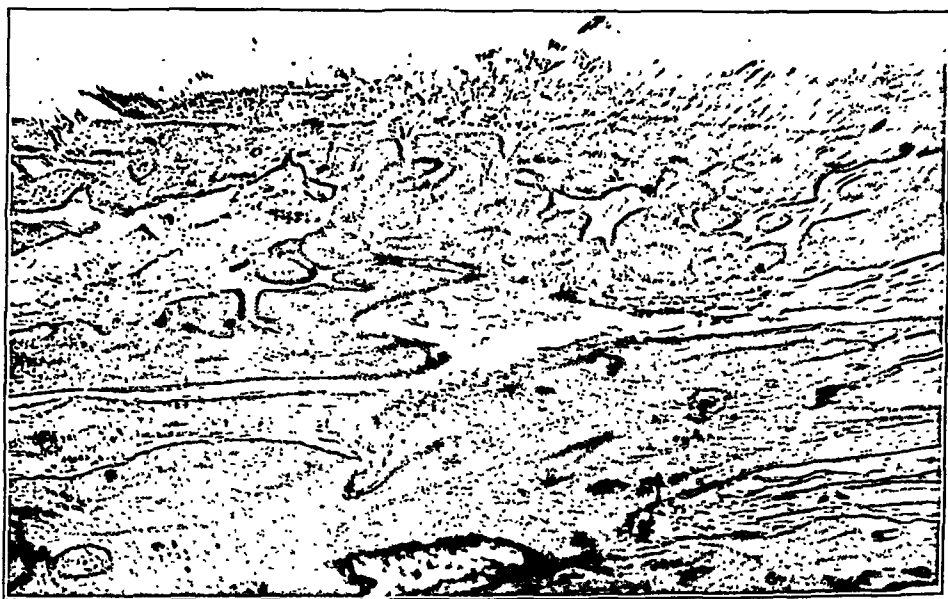


Fig. 13.—Cortex of right tibia (longitudinal section): a strip of adherent periosteum is present in the upper part of the picture (32 mm. objective).

pursue a tortuous course. Not infrequently the vessels are arranged in bundles of an artery and two or more veins. Each bundle is surrounded by a delicate connective tissue sheath, and several of these may be present in a large canal.

The walls of the arteries are normal in structure but are perhaps a little thinner than are normal arteries of the same size. The veins often appear widely dilated and their walls are extremely thin. In certain instances veins with a diameter of 1.5 mm. have walls that appear to be composed of only a single layer of endothelium which rests on the delicate connective tissue filling the canal. A striking asymmetry is present in the walls of some of the larger veins, one wall consisting of fifteen or more layers of cells and fibers while the opposite wall

consists of only a single layer of endothelium resting in a basement membrane of a few connective tissue cells and fibers.

In addition to the arteries and veins, a number of lymphatic vessels are present in the large canals. They are variable in size and all have thin walls. Some of them are empty, others contain a thin coagulum which stains like fibrin.



Fig. 14.—Right tibia (cross section): the area occupied by the wide canals is almost equal to that occupied by bone (16 mm. objective).

The groundwork of the connective tissue in the canals is made up of delicate collagenic fibers. They are not wavy and are not arranged in dense bundles as collagenic fibers elsewhere are. They form a loose network in the canal and in some areas are arranged in sheaves or whorls.

In sections stained by Weigert's method for elastic tissue a few dark brown or black fibers can be demonstrated in the loose connective tissue.

These fine elastic fibers tend to run parallel to the long axis of the canal, but may cross or even branch dichotomously.

The loose connective tissue is sparsely populated by cells. The majority of these appear to be young connective tissue cells or fibroblasts. They are spindle or stellate in shape with a large round or



Fig. 15.—Cortex of left tibia (longitudinal section): There are periosteum above, a wide canal in the center filled with delicate connective tissue and four small haversian canals near the surface (8 mm. objective).

oval vesicular nucleus and slightly eosinophilic cytoplasm. A moderate number of mature connective tissue cells with small deeply staining nuclei and thin elongated cell bodies also are present.

In addition to the fixed connective tissue cells a moderate number of round or ovoid wandering cells are present in the loose matrix. A

few of these are small lymphocytes. Others are slightly larger with round or ovoid nuclei and slightly basophilic cytoplasm (primitive cells or plasma cells or larger lymphocytes). The majority of these wandering cells are apparently monocytes with a large kidney shaped nucleus. Occasional osteoblasts and osteoclasts are seen lodged in the connective tissue far from the bony wall of the canal.



Fig. 16.—Cortex of left tibia (cross section of a large canal lined by osteoblasts and containing numerous blood vessels): the irregularities of the bone lamellae should be noted (8 mm. objective).

In a few of the larger canals small collections of fat cells are seen. The fat cells are most often found in those canals which communicate with the marrow cavity. The bone marrow extends a short distance into the canals and is gradually replaced by fat, which is in turn replaced by the myxomatous tissue described above.

In most places the walls of the large canals are lined by one or more layers of osteoblasts (fig. 16). These are usually arranged as a single layer of flattened or cuboidal cells but in some spots the bone is covered by three or four layers of cells and small pockets or recesses in the bone may be completely filled by osteoblasts. They have rather large, deeply staining nuclei and the protoplasm is like ground glass in appearance and stains a light purple in hematoxylin and eosin preparations. They resemble the osteoblasts of normal bone, but are present in greater number than osteoblasts in normal bone. In some areas the layer of osteoblasts is absent and the delicate connective tissue of the large canal is in direct contact with the bony framework. The smaller canals, which we regard as typical haversian canals, are not lined by osteoblasts.

A few osteoclasts are seen in most of the sections. They are large multinuclear cells whose nuclei and cytoplasm resemble the osteoblasts in staining characteristics except that both stain slightly deeper with the hematoxylin. They each contain from three to eight nuclei and as a rule lie on the surface of the bone wall or in Howship's lacunae, but may be free in the connective tissue.

The structure of the matrix of the bone is similar to that of normal bone except that the lamellae are very irregular in their arrangement. They are chiefly ground lamellae which run in every direction and apparently bear little relation to the course of the larger canals (fig. 16). In the thicker areas of bone, the smaller, or haversian, canals are usually surrounded by a series of concentric lamellae. In the case of the large canals the lamellae may run parallel to the wall of the canal, but more often than not they meet the canal at a right or an oblique angle and have no tendency to form concentric layers around the canal.

The organic matrix, like that of normal bone, is made up of alternating sheets of coarse collagenic fibers. Each sheet consists of a single layer of parallel fibers and the fibers in alternating layers tend to be at right angles to one another. In Weigert preparations an occasional dark brown elastic fiber is to be seen coursing through the bone matrix.

In the superficial portion of the cortex Sharpey's fibers are present. In sections stained with Mallory's phosphotungstic acid hematoxylin they are seen as coarse reddish brown collagenic fibers which run from the periosteum to the bone. They stain as does the bone matrix but can be traced for some distance into the bone, running through the layers of lamellae.

The bone cells are about as numerous as in normal cortical bone and lie in lacunae that have their long axes parallel to the enveloping lamellae. In the interlamellar areas where the groundwork has no definite structure the lacunae are shorter and thicker and may be roughly spherical in shape. In thinly ground sections of dried bone,

and in sections of decalcified bone stained by Schmorl's thionin method, the intercellular canaliculi are visible (fig. 17). These minute canals are thickly set around the periphery of the lacunae, running out in all directions, pursuing a wavy course, and uniting with the canaliculi from

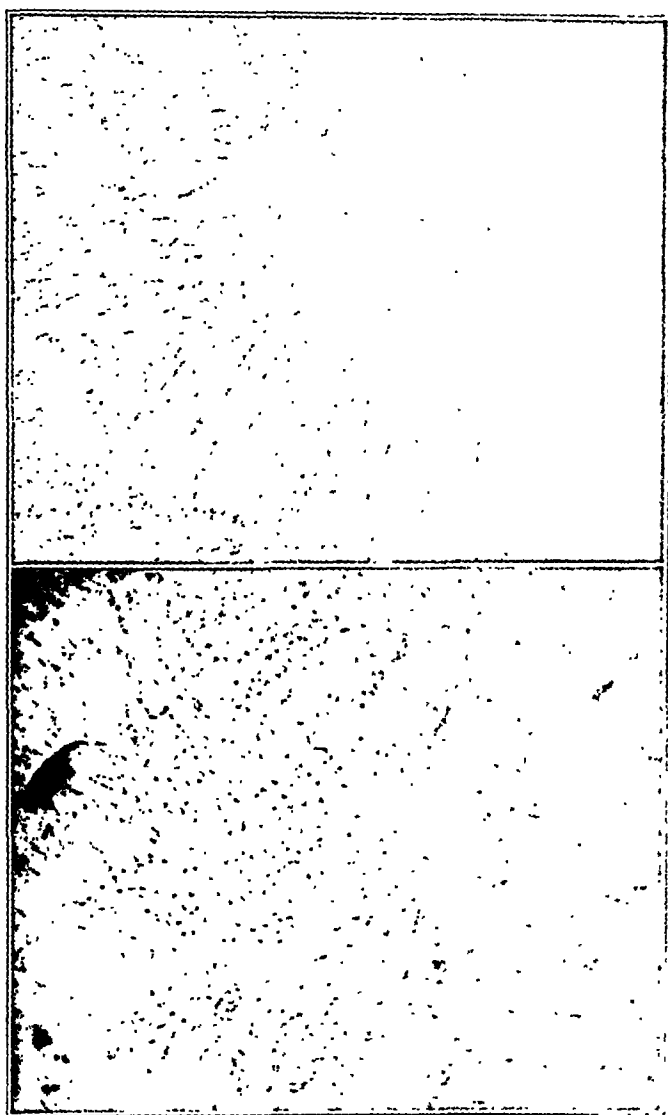


Fig. 17.—Bone lacunae and canaliculi stained by Schmorl's thionin method; in the upper picture the canaliculi pass from one lacuna to another; in the lower picture the canaliculi are mostly seen in cross section ($\times 2$ mm. oil immersion).

neighboring lacunae. In many instances canaliculi from two neighboring lacunae not only are continuous but send off branches that unite with similar branches from canaliculi on either side, thus forming a most intimate anastomosis. In properly stained sections the bone cells can

be seen to send protoplasmic processes into the canaliculi, and it is probable that in the living state the bone cells form a true syncytium; though I have not been able to demonstrate direct protoplasmic continuity between the cells in sections. In areas in which the lacunae are arranged in different planes, the canaliculi can often be traced across a row of lacunae in a different plane to unite with the canaliculi from the next-row that lie in the same plane. The lacunae that lie close to the large canals communicate with them by means of numerous canaliculi which open into the canals. This is true of both the haversian and the larger (Volkmann's) canals.

A section from the site of the nonunion in the right tibia presents a border of dense sclerotic bone 5 mm. in thickness. This sclerotic bone is not lamellated in structure and contains no canals or nutrient vessels. It is sparsely populated by cells. In some areas near its free border the cells are arranged in rows or nests as is typical of cartilage though here the matrix is definitely calcified.

Between the eburnated border zone and the rest of the shaft there is a zone of very atrophic bone where bone absorption and formation is in progress. The bone absorption is being carried on by osteoclasts which appear to be eroding some of the lamellae. The new bone is for the most part being formed by osteoclasts in the typical manner. In other areas the bone is being laid down in membrane or by calcification of connective tissue. A small calcified area is surrounded by a network of radiating fibers which gradually merge with the surrounding tissue of the large canals. From the center outward bone cells, osteoblasts and typical fibroblasts are met with. Apparently all transitions exist between these three types of cells.

At the operation the periosteum was found to be firmly adherent to the bone, but it was unusually friable and bits of it could be pulled off with tissue forceps. It was pinker and more delicate than is the fibrous periosteum of normal bone. Microscopically, it resembled normal periosteum and was composed of an outer fibrous and an inner reticular layer (fig. 18). The outer layer was made up of coarse, wavy collagenic fibers, most of which ran parallel to the long axis of the bone. It contained a moderate number of mature connective tissue cells. The inner layer was made up of delicate collagenic and elastic fibers which formed a loose reticulum. Here the connective tissue cells were more numerous and of a younger type than the lamellar cells of the outer layer. A few wandering cells also were present. Next to the bone cortex was a layer of osteoblasts. They resembled those of normal bone in size, number and arrangement. A number of coarse collagenic fibers from the outer layer crossed the reticular layer and extended into the bone (fibers of Sharpey). At the places where the large canals (Volkmann's) opened on the cortex, the reticular layer of

the cortex was continuous with the reticular tissue filling the canals, while the fibrous layer of the periosteum spanned the openings without dipping into the canals. The blood and lymph vessels lay in the reticular layer and were normal in size and number.

The tendon of achilles was unusually small, the diameter being about one-fourth inch. In the fresh state it was light pink and trans-



Fig. 18.—Cortex of left tibia (longitudinal section): The periosteum is shown above; the irregularity of the bone lamellae should be noted (8 mm. objective).

lucent in appearance. The dense white fibers of normal tendon were not present. On microscopic examination, both in cross and longitudinal sections the tendon appeared to be approximately normal. The fibers were normal in size and appearance, and were grouped in irregular bundles as are those of normal tendon. They reacted normally to the various connective tissue stains. There was perhaps a slight increase in the vascularity of the tendon, and the connective tissue cells were more numerous than usual but normal in size and arrangement.

body. These calcium metastases have not been noted by other observers, unless we consider the otosclerosis as being such.

A macular atrophy of the skin was present in the case of Blegvad and Haxthausen.³⁹ The patient was covered with grayish purple spots varying in size from minute spots up to areas 2 cm. in diameter. The base was smooth, sunken below the level of the surrounding skin, and the underlying veins were clearly visible. Microscopically there was an atrophy of the corium. In our case the skin was freckled and rather dry but otherwise normal.

Dentition is, as a rule, normal. In one of Voorhoeves' cases, the jaws were small and the lateral incisors were pointed inward. In the nonhereditary case of Vander Veer and Dickinson⁴⁰ the teeth were translucent and obviously lacked mineral salts, and the gums were spongy and bled easily. In Stobie's²⁴ family some of the members showed deficiencies in the enamel of the teeth and gave a history of the teeth breaking away on biting bread. Crocco⁴¹ noted late development of the teeth. In our case the teeth were normal.

Hemophilia was present in ten members of the large family studied by Voorhoeve. It has not been present in other families and is not yet proved to be a part of the syndrome.

The neurologic examination is as a rule negative and the intelligence is normal. The only exception in the literature is the case of brittle bones and blue sclera in a mongolian idiot reported by Bolten.⁴² (I am not sure that this case was of the hereditary type.)

Infant Mortality.—Bronson noted that in her family there was an abnormally high infant mortality rate among the affected members as compared with the normal members. In the family of Hass there were ten deaths in infancy or early life among the twenty-four persons. Tuberculosis was of frequent occurrence in the family of Voorhoeve.

Congenital Anomalies.—In one of the families of van der Hoeve and de Kleijn there were seven cases of syndactylism. Voorhoeve noted cleft palate three times, an adduction of the little fingers once, and rachischisis twice in his family. One of Blencke's cases had congenital torticollis.

39. Blegvad, O., and Haxthausen, H.: Blue Sclerotics and Brittle Bones, with Macular Atrophy of the Skin and Zonular Cataract, *Brit. M. J.* 2:1071 (Dec. 24) 1921.

40. Vander Veer, E. A., and Dickinson, A. M.: *Fragilitas Ossium*, *Ann. Surg.* 74:629 (Nov.) 1921.

41. Crocco: *Blau sklera*, *Comm. d. Hosp. Ophth. Buenos Aires* 2:38, 1920, quoted from Blencke.

42. Bolten, G. C.: *Het Voorkomen von blauwe Sclerae*, *Nederl. Tijdschr. v. Geneesk.* 1:560 (Feb. 23) 1918.

Laboratory Findings.—No abnormalities have been noted in the urine in these cases and none was present in our case. A number of authors have commented on the slight lymphocytosis present. In our case 34 per cent of the white blood cells were lymphocytes. We do not consider this unusual in a child. Thinking that perhaps there might be some abnormalities in the white blood cells, the blood was examined by the supravital technic several times. The living cells exhibited motility, contained the usual amount of mitochondria and reacted to neutral red as do the normal blood cells. The calcium and phosphorus content and the hydrogen ion concentration of the blood in our case were normal, the blood clotting time was normal and the basal metabolism was normal.

14. DIAGNOSIS, PROGNOSIS AND TREATMENT

The diagnosis is made by the presence of an abnormal bluish tint of the sclera which was also present in one or both parents. The presence, or absence of fractures or other stigmas is not necessary for the diagnosis.

The prognosis is that acute fractures will unite quickly. After the patient reaches the age of puberty it is probable that the fractures will cease to occur, though there are several cases on record in which fractures from minor forces have occurred in adult life. It is certain that if an affected person has children, approximately half the children will be afflicted with the condition.

Treatment.—The patient should be advised to lead a normal life but to refrain as much as possible from subjecting the bones to trauma. Drugs, chemotherapy, vitamins, diet, light rays and endocrine preparations have been tried. No form of treatment is known to have any effect on the condition. Acute fractures should be treated just as though the patient were normal. The treatment should be prompt and the period of immobilization can be shortened, as the bones tend to unite quickly. Deformities, if present, should be corrected. These patients stand operations well and there is no cause to fear nonunion after osteotomies. As a measure of prevention these unfortunate persons should be told that if they marry and have children at least half the children may be expected to be afflicted with hypoplasia of the mesenchyme.

15. COMMENT

The term "hereditary hypoplasia of the mesenchyme" is used to describe the condition usually called brittle bones and blue sclera. This is because it has been shown that in these cases many of the mesenchymal tissues may be underdeveloped.

This type of fragilitas ossium is hereditary and in addition to the brittleness of the bones is characterized by blue sclera, small stature,

hypermobility of the joints and a weakness of the fibrous structures throughout the body. The cases that reach adult life tend to develop progressive deafness.

The hereditary factor is a dominant one. The condition is inherited directly from an affected parent. Of children one of whose parents is affected with blue sclera, 62 per cent are born with blue sclera and 42 per cent suffer multiple fractures. There is no skipping of generations and the children of affected parents who are themselves not affected do not transmit the condition to their offspring.

The blue appearance of the sclera is not due to a deposit of pigment but is due to an abnormal translucency of the fibrous tissue which permits a shining through of the deeper tissues. From observations in the fascia and tendons in our case it is probable that the sclera is thinner than normal and is of an abnormal quality.

The fractures in these cases are not spontaneous but are due to definite causes. In most instances, however, the violence causing the fracture is less than would be necessary to break a normal bone. The deformities are due to malunion of old fractures and not to softening of the bone. Roentgenograms of the skeleton in our case showed a general decrease in the size of the bones, a thinning of the skull, and a concentric atrophy of the long bones.

There was cortical striation of compact bone and coarseness of structure of spongy bone. The bones that had not been subject to disuse showed little rarefaction. There are cases in the literature in which the bones are reported as being rarefied and exhibiting eccentric atrophy. Whether or not the two types occur in the same family is not known. There have been no adequate roentgenographic reports on several members of a family. Such studies are needed to clear up this phase of the subject.

Examination of the bone removed at operation from our patient showed it to be unusually hard and brittle. The structure was similar to that of normal bone except that the lamellae were irregular in arrangement and the amount of compact bone was decreased by the presence of numerous large canals. The cortex of the tibia was honeycombed with large canals which contained a very vascular connective tissue.

The presence of these canals explains the cortical striations seen in the roentgenograms. They also partly explain the ease with which the bones are fractured. The irregularity of the lamellae probably renders the bone less strong than normal. A third factor is the probability that there is some abnormality in the quality of the fibrous matrix of the bone. This is suggested by the observation that the tendon of achilles was pink and translucent in appearance and much reduced in diameter: on microscopic examination, however, the fibrous structure of the tendon was normal in appearance. The nature of the abnormality in

the quality of the fibrous tissue is not known. It is probable that it involves all the collagenic tissue in these patients and explains the friability of the blood vessels, fascia, periosteum and subcutaneous tissues noted in our case.

The rapid healing of the fractures in these cases is explained by the presence of large numbers of osteoblasts in the wide canals of the cortical bone.

The blood of our patient was examined several times and the hydrogen ion concentration and calcium and phosphorus content were always within normal limits. The p_H tended to the alkaline side of the normal range and the calcium and phosphorus tended to be a little high.

From our studies hypoplasia of the mesenchyme seems to be an anomaly of development rather than a derangement of metabolism. The hypoplasia is apparently limited to those tissues derived from the mesenchyme. We have found no evidence of any endocrine disturbance in our patient. It is certain that the condition exists in varying degrees in different individuals who are affected with the hereditary type of blue sclera. It is probable that those who have not had fractures have abnormalities in the structure of the bones similar to those present in our case. That they have not had fractures is due either to the condition being less in degree or to the fact that the bones have been subjected to less trauma.

From what has been said above it is probable that hereditary hypoplasia of the mesenchyme is in no way related to any of the acquired forms of bone fragility. We have then to consider its possible relation to osteogenesis imperfecta and to idiopathic osteopsathyrosis. In spite of the opinions of numerous German authors that these two conditions have the same pathologic basis, it seems better to consider them as separate conditions because they certainly present different clinical pictures.

In regard to osteogenesis imperfecta, it is to be noted that this condition is not known to be hereditary. The typical patient is born of apparently normal parents and presents numerous fractures at birth or in infancy. Most of the patients die in infancy and so cannot transmit the condition. Furthermore, no case of osteogenesis imperfecta has been recorded in any of the families afflicted with hereditary hypoplasia of the mesenchyme.

In idiopathic osteopsathyrosis the fractures occur in childhood and are not as a rule numerous. It is known that some of these patients have blue sclera, and it is probable that they also present other evidence of hypoplasia of the mesenchyme, though this has not been noted in any of the cases reported. The few reports on the bone in this condition resemble the pathologic findings in our case. In brief, our case resembles closely some of the reported cases of idiopathic osteopsathyrosis. The

only known difference is that in our case the condition is a dominant hereditary character. To settle the question of the identity of the two conditions we need a patient with idiopathic osteopsathyrosis with blue sclera and born of normal parents who has transmitted the condition to some of his or her children.

On the other hand, there are cases of nonhereditary idiopathic osteopsathyrosis with sclera of normal color.⁴³ The question as to whether or not these form a separate group cannot be decided at this time. It is certain, however, that they do not fit into the group which we term hereditary hypoplasia of the mesenchyme.

A fourth and rare type of idiopathic bone fragility is that known as marble bones, or Albers-Schonberg disease. It is probably not hereditary.⁴⁴ This is not usually classed as a type of fragilitas ossium but the hardness and brittleness of the bones noted in our case are at least suggestive that the two conditions have some features in common.

From what has been said in the foregoing it is possible to classify idiopathic bone fragility as follows:

1. Hereditary Form: Hereditary hypoplasia of the mesenchyme.
2. Nonhereditary Forms: (a) Osteogenesis imperfecta; (b) osteopsathyrosis with white sclera; (c) osteopsathyrosis with blue sclera.
3. Probably Not Hereditary: Osteosclerosis fragilis generalisata, or marble bones.

16. SUMMARY

From an analysis of the literature it is shown that blue sclera is the only feature of hereditary hypoplasia of the mesenchyme which is present in every case and which is transmitted as a dominant hereditary character.

The other abnormalities are short stature, brittle bones, hypermobility of joints and deafness.

Our observations lead us to believe that idiopathic fragility of bones is due to an abnormality in development rather than to a metabolic disturbance.

43. Glover, D. M.: Osteopsathyrosis, Arch. Surg. 5:464 (Nov.) 1922.

44. Davis, G. G.: Osteosclerosis Fragilis Generalisata, Arch. Surg. 5:449 (Nov.) 1922.

comprehended under the term of vertebral epiphysitis are causes of static disturbance.

Finally, as further evidence that vertebral epiphysitis is a cause of spinal deformity, I wish to present two previously reported cases with additional data.

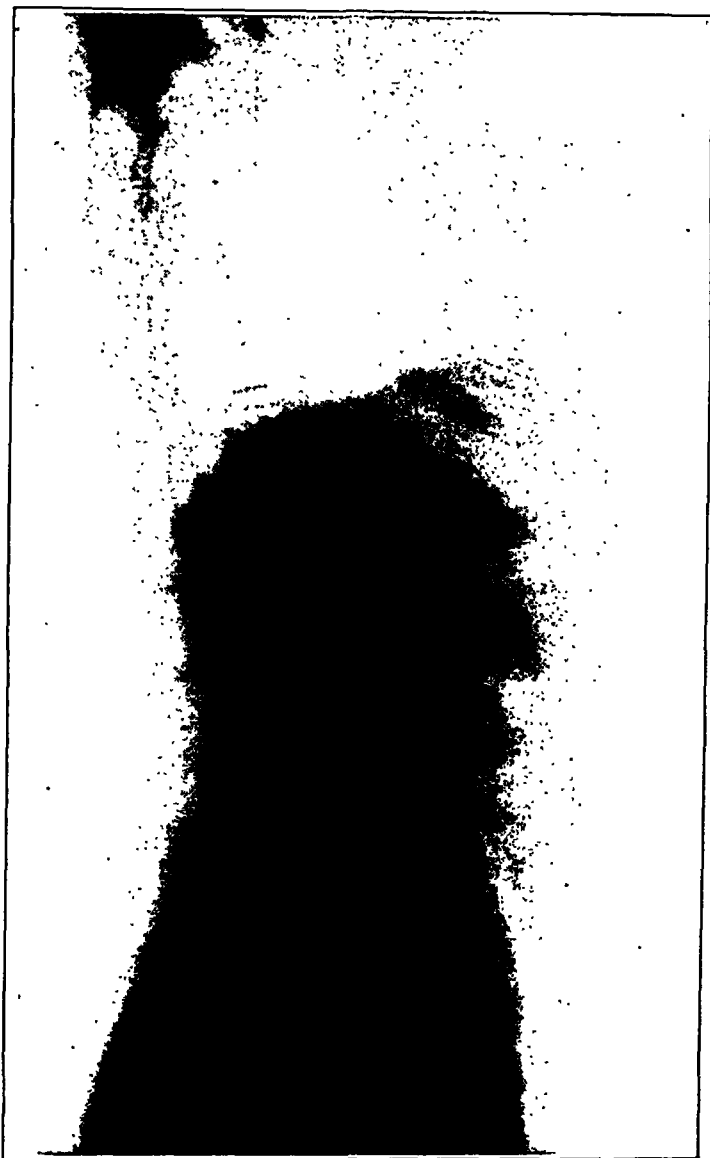


Fig. 1 (case 1).—Lateral view, April 20, 1924, showing normal dorsal and lumbar curves, mottling and haziness of upper dorsal intervertebral spaces, indistinct and irregularly thickened upper and lower outlines of dorsal vertebrae and thickened posterior epiphyses; comparison should be made with figure 2.

REPORT OF CASES

CASE 1.—E. B., a girl, aged 13 years and 7 months, was admitted to the Hospital for the Ruptured and Crippled in the service of Dr. Royal Whitman because of scar contractions of several of her fingers subsequent to an injury. Her

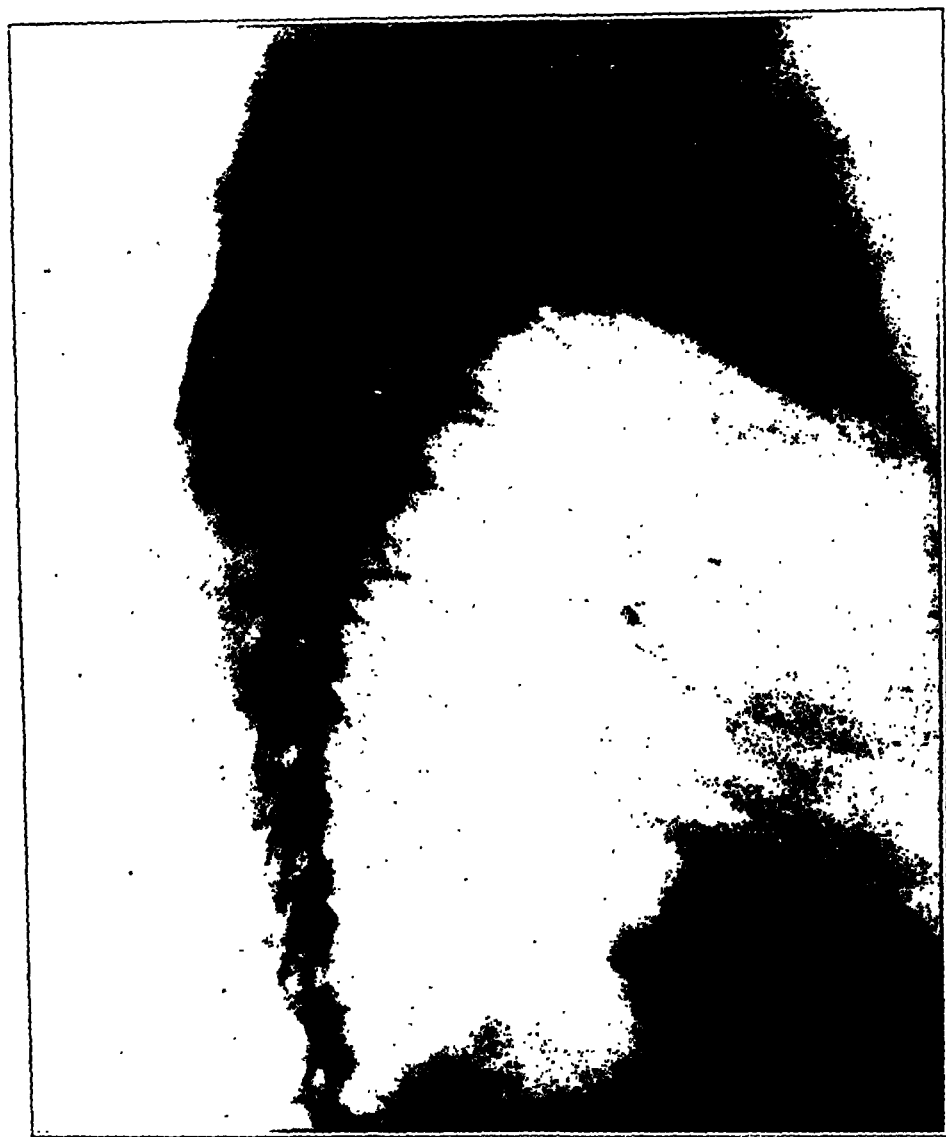


Fig. 2 (case 1).—Oblique lateral view of dorsal region, Feb. 28, 1925, showing mottling of intervertebral spaces and irregularly thickened, moth-eaten, hazy appearance of superior and inferior outlines of vertebral bodies and superior and inferior epiphyses, i. e., an increase in the roentgenologic pathologic condition.

history was irrelevant save that she had had "growing pains" in the knees and elbows on excessive exertion. Clinically, her back was symmetrical and her spine was negative in all respects.

She was thought a fit subject for our study of normal spines, and consequently was roentgenographed, April 30, 1924. Much to our surprise and temporary confusion the roentgenograms showed in the anteroposterior views that beginning



Fig. 3 (case 1).—Lateral view, Jan. 5, 1926, showing an increase in dorsal and lumbar curves and an increased wedging of dorsal vertebrae.

with the fifth and down to and including the twelfth dorsal vertebrae, the superior and inferior borders of the vertebral bodies were not as distinct as elsewhere, and the intervertebral spaces were diminished, fogged and mottled. The lateral views showed no abnormality in the anteroposterior curves. The twelfth dorsal vertebra was somewhat wedge shaped. On the superior border of the eleventh dorsal vertebra, there was a faint irregular linear thickening which was interrupted

anteriorly. The same was present on the inferior border of the tenth dorsal vertebra, only more distinct. In the ninth intervertebral space, the superior and inferior posterior thickenings were marked and they extended anteriorly as broken lines. The same findings were present in the eighth dorsal intervertebral space. In the seventh, sixth, fifth and fourth dorsal intervertebral spaces the epiphyseal plates were very much thickened, their outlines were indistinct, they were fragmented and the interspaces were mottled and hazy. The superior and inferior borders of all these vertebral bodies were indistinct and irregular (fig. 1).

Feb. 28, 1925, the patient and her mother volunteered the information that they had noticed a tendency to round shoulders. Clinically there was a mild degree of round shoulders which was not present at the first examination. There was definite tenderness over the sacrococcygeal junction and both iliac crests. Roentgenograms

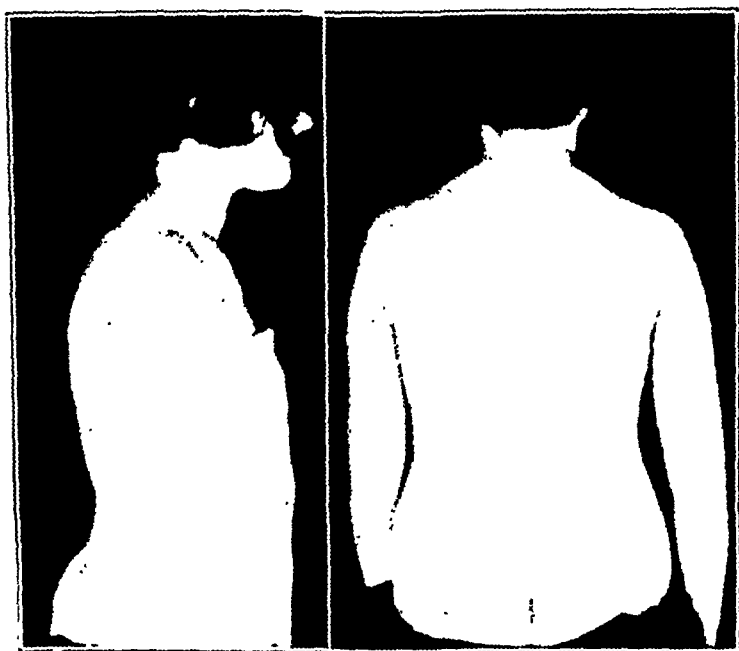


Fig. 4 (case 1).—Appearance of patient, Jan. 5, 1926, showing a moderate grade of round shoulders, which was absent when the patient came under observation.

taken at this time showed an advance in the pathologic condition described and an increase in the normal dorsal curve (fig. 2).

When seen, October 10, the patient had no complaint referable to the spine. Clinically the back was negative save for an increase in the kyphos in the lower dorsal region. Roentgen-ray examination substantiated the increase in curvature. The epiphyseal pathologic condition had changed but slightly since the last examination.

The patient was last seen, Jan. 5, 1926, when no further changes were noted (figs. 3 and 4).

CASE 2.—A. D., a boy, aged 15 years, was admitted to the Hospital for the Ruptured and Crippled in the service of Dr. Royal Whitman for treatment for rigid flatfoot. He had recently arrived from Austria where he had undergone a great deal of starvation and privation. He was underweight, tall for his age and somewhat anemic. There was no history referable to his spine and clinically his back was negative.

He was roentgenographed, May 20, 1924, for our normal series of spines. The anteroposterior view showed that beginning with the seventh and down to the twelfth dorsal vertebra, there was a mottled haziness in the intervertebral spaces which were irregular in size. The upper and lower vertebral outlines were indistinct and appeared moth-eaten. In the intervertebral spaces there were definite darker and lighter areas very much akin to the appearance in Legg's disease. The

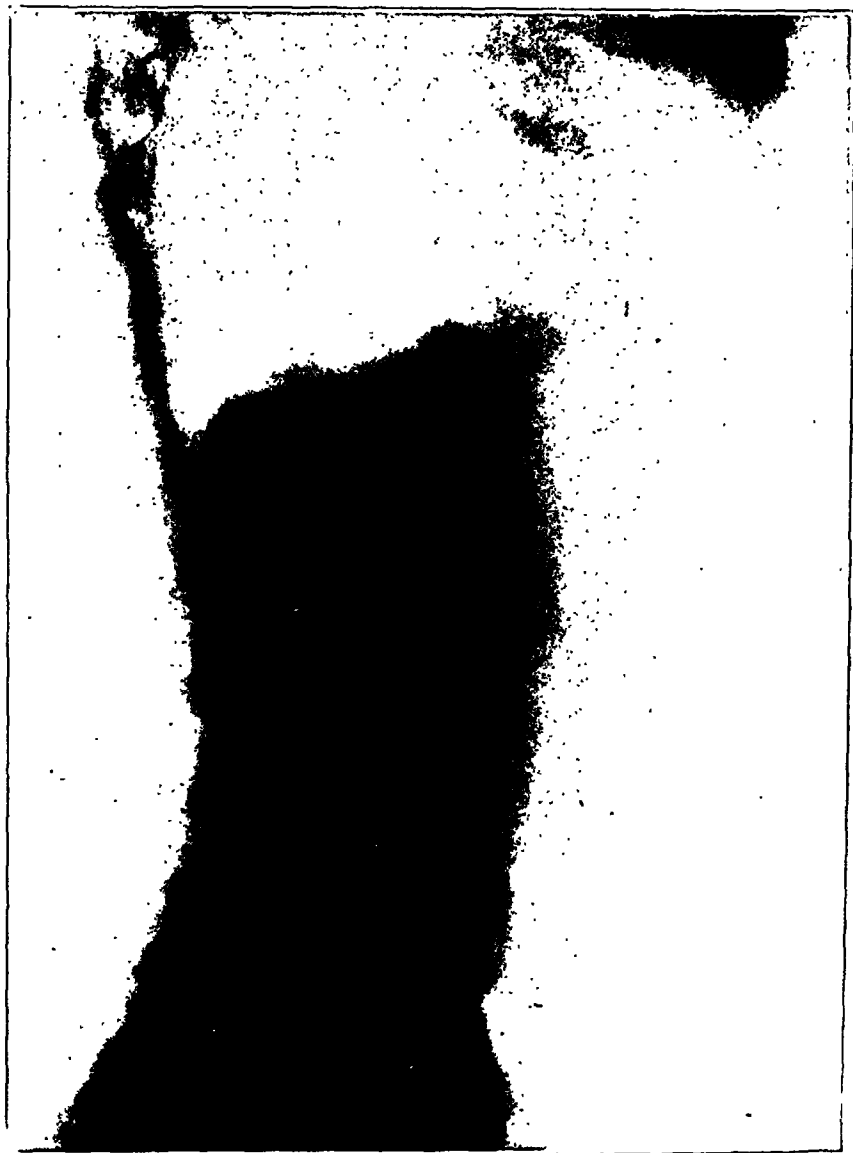


Fig. 5 (case 2).—Lateral view, May 20, 1924, showing normal dorsal and lumbar curves, enlarged, frayed and irregular epiphyses in the dorsal region with mottling and haziness of the intervertebral spaces.

lateral view showed normal anteroposterior curves. From the seventh dorsal down to the inferior border of the eleventh dorsal vertebra the anterior inferior and superior, and the posterior inferior and superior epiphyseal plaques were much enlarged, so that there were distinct concavities just behind the anterior and just in front of the posterior plaques, while the intervening areas were convex. All the

outlines were poorly demarcated and within the spaces there were darker and lighter areas. In addition, the vertebral bodies appeared more porous than in the lumbar region, which were apparently negative (fig. 5).

When the patient was seen, March 7, 1925, he complained of occasional fleeting pains in the cervical portion of the spine. He also noted that he had grown considerably during the interval. Examination showed that his posture was poor.



Fig. 6 (case 2).—Lateral view of dorsal region, Oct. 10, 1925, showing an increase in dorsal curve, wedging of vertebral bodies, irregularity, moth-eaten and indistinct appearance of epiphyses and superior and inferior vertebral outlines.

There was a definite round shoulders hollow back present. Roentgen-ray examination showed an increase in the dorsal kyphosis and the lumbar lordosis. The eighth and ninth dorsal vertebrae were wedged. The vertebral outlines were now sharper, denser and less wavy. The epiphyseal plaques were less thickened, less frayed and less moth-eaten. The intervertebral spaces showed considerable striation and mottling.

Examination, October 10, showed a further increase in growth and a more marked hollow round back. Röntgenograms showed an increase in the deformity. The middorsal region showed more wedging of the bodies and some increase in the pathologic change shown in the roentgenogram. The upper dorsal region was somewhat improved (fig. 6).

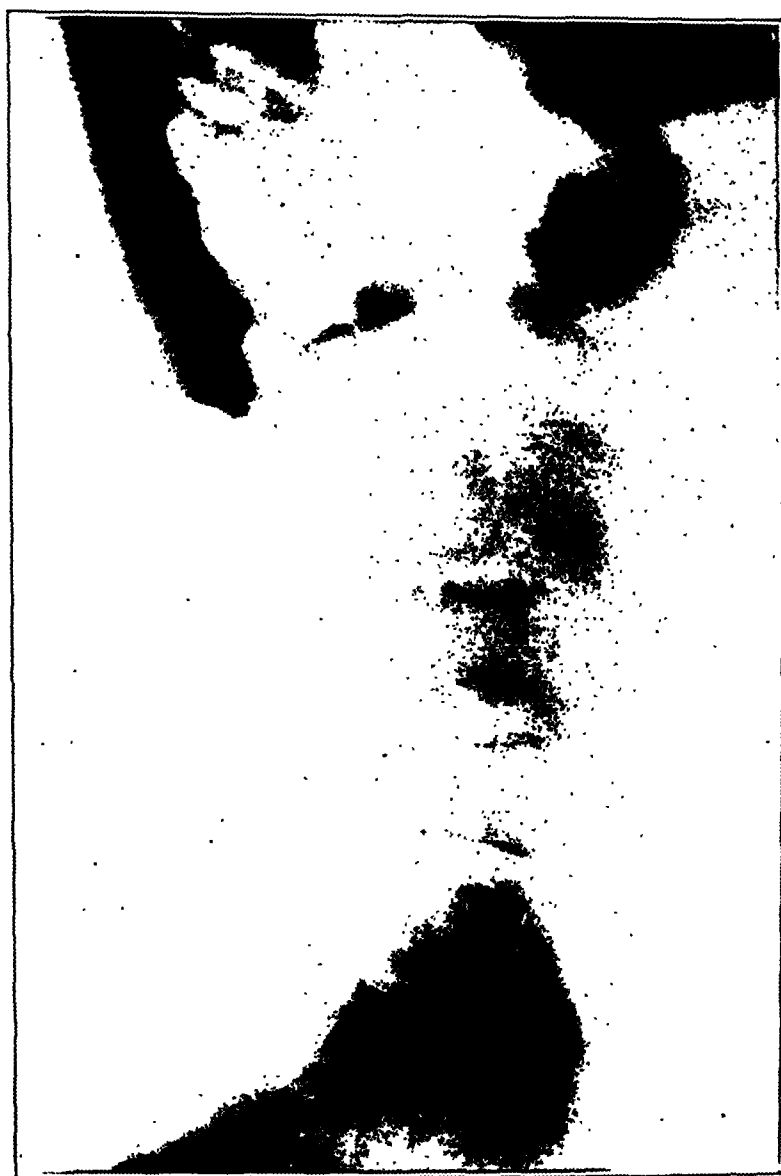


Fig. 7 (case 2).—Lateral view, Jan. 13, 1926, showing further increase in dorsal and lumbar curves; comparison should be made with figure 5.

Jan. 13, 1926, the patient had no complaints. The hollow round back was more marked (fig. 8). The roentgenograms showed an increased kyphosis with an increase in the wedging at the apex of the dorsal curve. The epiphyses could not be distinguished as such (fig. 7).

In reviewing these two cases it is evident (1) that when first observed they presented negative anamneses, negative clinical appearances and a

definite roentgenologic pathologic condition without gross deformities of the spine; (2) that while under observation some clinical evidences of epiphyseal derangements appeared, namely, occasional pain, tenderness and rapid growth in the second case, and (3) that deformity finally developed.

CONCLUSIONS

1. Vertebral epiphysitis is not found in deformities of the spine of known origin, such as poliomyelitis, Pott's disease, rickets, torticollis, congenital deviations and inequality of the lower limbs.

2. The active or acute stage of vertebral epiphysitis is more commonly seen in the milder deformities and less commonly in the severe



Fig. 8 (case 2).—Appearance of patient, Jan. 13, 1926, showing a marked hollow round back; when the patient came under observation this condition was not present.

deformities. All that usually remains in the severe deformities are the end-results.

3. Vertebral epiphysitis causes a derangement in the epiphyses which starts a cycle of events in accordance with Delpêche's Law and the pathogenesis of the resultant spinal deformities is the same as in rickets, poliomyelitis and Pott's disease.

4. In the two cases with negative clinical and definite roentgenologic symptoms presented, the patients subsequently developed deformities.

5. From the foregoing observations it is my belief that vertebral epiphysitis is a competent cause of spinal deformity.

EXPERIMENTAL ACUTE GASTRIC FISTULA

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Changes that occur in the blood in experimental acute gastric fistula are a rise in the carbon dioxide combining power of the plasma, a decrease in chlorides, and an increase in urea. These changes are similar in some respects to those in acute duodenal fistula¹ and to those other observers² have found in high intestinal stasis. In experimental acute gastric fistula there is a greater increase in blood alkalinity, as denoted by the carbon dioxide combining power of the blood, due to the loss of acid from the body through the gastric fistula. The decrease in the chloride content of the blood is quite comparable to that in duodenal fistula and in high intestinal stasis. Studies of the fistulous fluid revealed a loss of chlorides sufficient to account for the decreased chloride content of the blood. Because of the pronounced decrease in blood chlorides and the beneficial results obtained by the use of chloride in high intestinal stasis and also in duodenal fistula, we have studied the effect of intravenous injections of chloride solutions in comparison with other control solutions in gastric fistula. Of the various solutions, isotonic sodium chloride solution compensated best for the chemical changes in the blood accompanying acute gastric fistula and assisted most in prolonging life. The amount of nitrogen lost in the urine and in the fistulous fluid remained at approximately the normal level, although there was definite evidence of the retention of nitrogen in the blood.

1. Walters, Waltman; Kilgore, A. M., and Bollman, J. L.: Changes in the Blood Resulting from Duodenal Fistula: A Clinical and Experimental Study, *J. A. M. A.* **86**:186-189 (Jan. 16) 1926.

2. Brown, G. E.; Eusterman, G. B.; Hartman, H. R., and Rowntree, L. G.: Toxic Nephritis in Pyloric and Duodenal Obstruction: Renal Insufficiency Complicating Gastric Tetany, *Arch. Int. Med.* **32**:425-455 (Sept.) 1923. Haden, R. L., and Orr, T. G.: Chemical Changes in the Blood of the Dog After Pyloric Obstruction, *J. Exper. Med.* **37**:377-381 (March) 1923; Chemical Changes in the Blood of the Dog After Obstruction of the Esophagus and of the Cardiac End of the Stomach, *J. Exper. Med.* **38**:477-485 (Oct.) 1923. McVicar, C. S.: A Discussion of the Clinical and Laboratory Findings in Certain Cases of Obstruction in the Upper Gastro-Intestinal Tract: The Role of Blood Chemistry in Diagnosis, Prognosis and Treatment of This Condition, *Am. J. M. Sc.* **169**:224-235 (Feb.) 1925.

Just before death a decrease in the excretion of nitrogen occurred accompanying anuria.

The work of Haden and Orr³ in experimental high intestinal obstruction showed that the nearer the obstruction to the pylorus the greater the toxemia, which might be explained on the hypothesis that the loss of chlorides in such cases was due to their excretion into the lumen of the stomach and the intestine and loss from the body in that manner, whereas in experimental fistula the chlorides were lost from the body through the fistula. Again, in experimental acute gastric fistula as in acute duodenal fistula, a part is played by interruption in the continuity of the gastro-intestinal tract by the gastric fistula. Studies are now being carried out in an attempt to evaluate the effect of discontinuity of the gastro-intestinal tract.

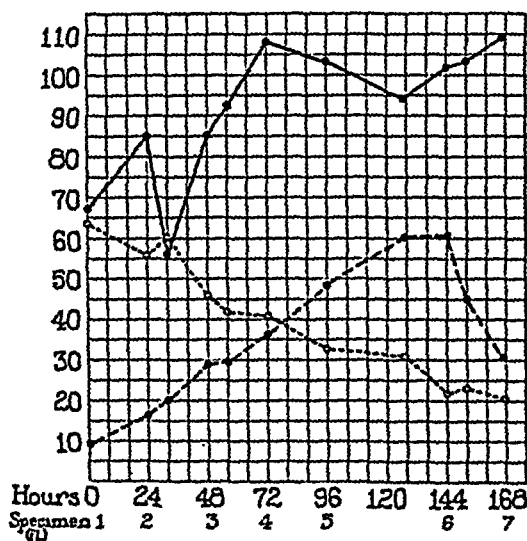


Chart 1.—Chemical changes in the blood in dog with gastric fistula following administration of water through duodenal tube: solid dot solid line, carbon dioxide; solid dot broken line, urea; open dot broken line, chlorides.

METHODS

Gastric fistulas were made on dogs under ether anesthesia, the stomach being isolated and divided at the pylorus. The duodenal stump was turned in as a blind end and the pyloric end of the stomach incorporated in the closure of the abdominal wound, producing a complete gastric fistula. In certain animals, other fistulous openings were made in the intestine by attaching the cut edge of the intestine to the incision. In others a T tube was introduced into the intestine

3. Haden, R. L., and Orr, T. G.: The Effects of Sodium Chloride on the Chemical Changes in the Blood of the Dog After Pyloric and Intestinal Obstruction, *J. Exper. Med.* 38:55-71 (July) 1923.

for the administration of fluids. A portion of the gastric wall was incorporated in the abdominal incision of one dog, and complete and partial gastrectomy, respectively, were performed on dogs as control experiments. In other dogs the proximal end of the duodenum was closed after complete or partial gastrectomy had been performed. Specimens of blood were obtained from the jugular vein at appropriate intervals, and the animals were kept in metabolism cages, urine and fistulous fluids being collected once in about twenty-four hours. The

TABLE 1.—*Chemical Changes in Blood, Urine and Fistulous Fluid of Dog with Gastric Fistula (Water by Duodenal Tube)*

| Date, 1925 | | Hours Following Operation | Blood | | |
|------------|--|---------------------------|------------------------------------|-------------------------------------|--------------------------------|
| | | | Carbon Dioxide, per Cent by Volume | Urea Nitrogen, Mg. for Each 100 Cc. | Chloride, Mg. for Each 100 Cc. |
| 3/3..... | | 0 | 67.1 | 9.9 | 633 |
| 3/4..... | | 23 | 85.5 | 16.6 | 561 |
| 3/4..... | | 31 | 57.4 | 20.2 | 608 |
| 3/5..... | | 48 | 85.5 | 28.2 | 466 |
| 3/5..... | | 56 | 93.5 | 28.4 | 425 |
| 3/6..... | | 72 | 108.4 | 36.4 | 410 |
| 3/7..... | | 97 | 103.3 | 48.7 | 330 |
| 3/8..... | | 126 | 94.7 | 60.1 | 311 |
| 3/9..... | | 144 | 102.3 | 61.4 | 220 |
| 3/9..... | | 152 | 103.3 | 45.3 | 239 |
| 3/10..... | | 168 | 109.9 | 30.0 | 209 |

| Date, 1925 | | Specimen | Volume, Cc. | Period of Collection of Sample, Hours | Urine | | |
|------------|--|----------|-------------|---------------------------------------|------------------------------------|---------------------------------------|-------------------------------|
| | | | | | Urea Nitrogen, Mg. in Total Sample | Ammonia Nitrogen, Mg. in Total Sample | Chloride, Mg. in Total Sample |
| 3/3..... | | 1 | 40 | 7.5 | 668.4 | 10.0 | 200.8 |
| 3/4..... | | 2 | 250 | 16.5 | 1,670.0 | 530.0 | 1,478.5* |
| 3/5..... | | 3 | 350 | 24.0 | 3,430.0 | 910.0 | 1,354.5* |
| 3/6..... | | 4 | 260 | 24.0 | 1,374.0 | 650.0 | 661.4* |
| 3/7..... | | 5 | 350 | 24.0 | 1,012.0 | 2,026.0 | 287.0* |
| 3/9..... | | 6 | 900 | 48.0 | 3,276.0 | 3,924.0 | 1,986.0* |
| 3/10..... | | 7 | 500 | 24.0 | 1,620.0 | 1,480.0 | 1,670.0* |

| Date, 1925 | | Specimen | Volume, Cc. | Period of Collection of Sample, Hours | Fistulous Fluid* | | |
|------------|--|----------|-------------|---------------------------------------|------------------------------------|---------------------------------------|-------------------------------|
| | | | | | Urea Nitrogen, Mg. in Total Sample | Ammonia Nitrogen, Mg. in Total Sample | Chloride, Mg. in Total Sample |
| 3/3..... | | 1 | 350 | 7.5 | 10.5 | 10.5 | 651.0 |
| 3/4..... | | 2 | 180 | 16.5 | 0.9 | 9.0 | 903.0 |
| 3/5..... | | 3 | 450 | 24.0 | 24.5 | 18.0 | 1,352.7 |
| 3/6..... | | 4 | 250 | 24.0 | 2.5 | 20.0 | 1,467.5 |
| 3/7..... | | 5 | 200 | 24.0 | 12.0 | 20.0 | 902.0 |

* The urine obtained by catheterization was added to that of the metabolism cage. The high chloride content is due to the mixture with the fistulous fluids. The fistulous fluid is only that which could be obtained without urinary contamination.

blood urea was determined by the method of Van Slyke and Cullen,⁴ the carbon dioxide combining power of the blood plasma by the Van Slyke method,⁵ and the blood plasma chlorides by the method of Whitehorn.⁶

4. Van Slyke, D. D., and Cullen, G. E.: A Permanent Preparation of Urease, and Its Use in the Determination of Urea, *J. Biol. Chem.* 19:211-228, 1914.

5. Van Slyke, D. D., and Cullen, G. E.: I, The Bicarbonate Concentration of the Blood Plasma; Its Significance and Its Determination as a Measure of Acidosis, *J. Biol. Chem.* 30:289-346 (June) 1917.

6. Whitehorn, J. C.: Simplified Method for the Determination of Chlorides in Blood or Plasma, *J. Biol. Chem.* 45:449-460, 1920.

The urea content of the urine and fistulous fluids was determined by the method of Marshall⁷ as modified by Van Slyke and Cullen.⁸ The chlorides in the urine and fistulous fluids were determined by a slightly modified Volhard-Arnold method.⁹

CHANGES IN THE BLOOD

Following the production of experimental acute gastric fistula, the average rise of the carbon dioxide combining power of the blood plasma was 55 per cent by volume in animals receiving only moderate amounts of water by rectum and none intravenously. For example, in Dog H788 (chart 1, table 1), the carbon dioxide combining power of the blood rose within the first twenty-four hours after operation from a preopera-

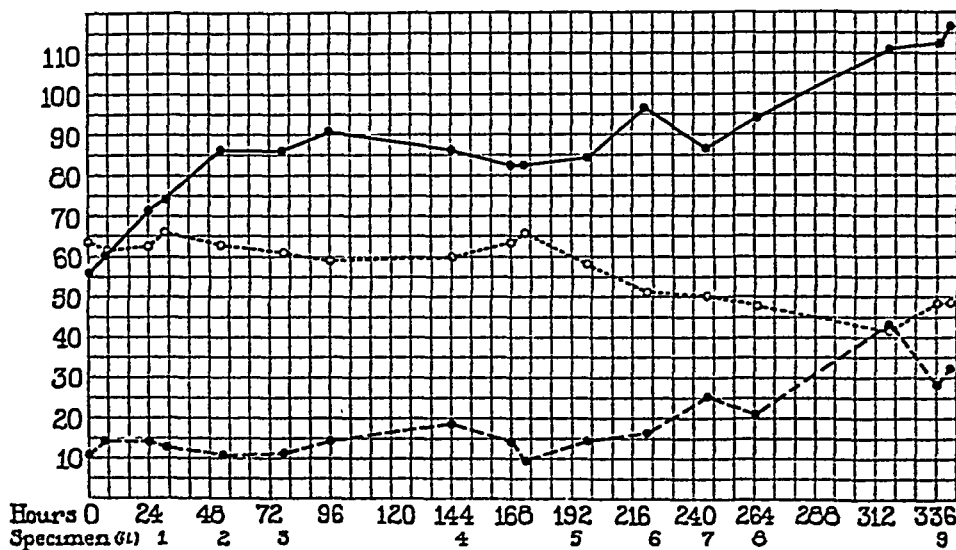


Chart 2.—Chemical changes in the blood in dog with gastric fistula following physiologic sodium chloride solution intravenously: solid dot solid line, carbon dioxide; solid dot broken line, urea; open dot broken line, chlorides.

tive level of 67.1 per cent by volume to 85.5 per cent by volume. Eight hours later, following the administration of fairly large amounts of water by duodenal tube, the carbon dioxide combining power was 57.4 per cent by volume. This rose within the next sixteen hours to 85.5 per cent by volume, and remained at this high level or above until it

7. Marshall, E. K.: A Rapid Clinical Method for the Estimation of Urea in Urine, *J. Biol. Chem.* **14**:283-290, 1913; The Determination of Urea in Urine, *J. Biol. Chem.* **15**:495-496, 1913; On Soy Bean Urease: The Effect of Dilution, Acids, Alkalis and Ethyl Alcohol, *J. Biol. Chem.* **17**:351-361, 1914.

8. Van Slyke, D. D., and Cullen, G. E.: A Permanent Preparation of Urease, and Its Use for Rapid and Accurate Determination of Urea, *J. A. M. A.* **62**: 1558-1559 (May 16) 1914.

9. Folin, Otto: Laboratory Manual of Biological Chemistry, with Supplement, ed. 3, New York, D. Appleton & Co., 1922.

increased to the maximum of 109.9 per cent by volume on the day of the dog's death. The decrease in plasma chlorides was equally striking. Within the first twenty-four hours after operation a decrease was noted, although some variations occurred within the first day or two. Following this period of adjustment, there was a progressive decrease until on the third day after the production of the fistula the chloride content was only two-thirds the normal amount. From this point, the decrease was continuously progressive so that only one-third the normal amount was present before the death of the animal. The changes in the urea nitrogen of the blood were somewhat more variable than those in the carbon dioxide combining power and the chloride content. In general, the urea content increased progressively and appeared to be greater when the plasma chlorides were at their lower levels. Its variations may be well accounted for by variations in the amount of nitrogen excreted by the kidneys, due to conditions in the kidneys, to fluid intake, or to the rate of urea formation. In dogs receiving small amounts of fluid there seemed to be a high concentration of urea in the blood, whereas increases in the fluid intake resulted in a lower level, and a normal level of blood urea was maintained only with great difficulty.

EFFECT OF SOLUTIONS GIVEN INTRAVENOUSLY

The effect of intravenous injections of large amounts of physiologic sodium chloride solutions was noteworthy. With the injection three times a day of 25 cc. for each kilogram of body weight, the life of animals with acute gastric fistula could be prolonged several days (chart 2, table 2). However, the carbon dioxide combining power of the blood remained at a high level. With the discontinuance of the injections, although a large quantity of water was supplied by mouth, characteristic changes in the blood recurred. Following the intravenous injections of comparable amounts of 5 per cent glucose solution, animals with gastric fistula appeared to be in slightly better condition than those receiving only water. There was less concentration of blood urea than in animals receiving water, and more concentration than in those receiving sodium chloride solution of similar tonicity. The decrease in the chlorides of the blood did not seem to be affected by the intravenous injections of glucose solution, as the decrease was the same as in the other animals except those to which chlorides were given. The increase in the carbon dioxide combining power of the blood was likewise not affected by the injection of this solution, since the rise was essentially the same in these animals as in the other untreated animals of the series. The life of the animals was maintained but little longer than that of those receiving water. Intravenous injections of 2 per cent sodium sulphate solution (25 cc. for each kilogram of body weight, three times a day) produced effects almost identical with those of glucose solutions of the same

tonicity (5 per cent). In these animals the urea of the blood continued to rise, the chloride content decreased, and the carbon dioxide combining power increased to the usual high level in animals with gastric fistula. The prolongation of life did not differ materially from that in animals receiving water or glucose solution intravenously.

TABLE 2.—*Effects of Physiologic Sodium Chloride Solution on Chemical Changes in Blood, Fistulous Fluid and Urine of Dog with Gastric Fistula*

| Date, 1925 | Time | Blood | | | Remarks | |
|---------------------------|-------------|------------------------------------|---------------------------------------|-------------------------------------|---|--------------------------------|
| | | Carbon Dioxide, per Cent by Volume | Urea Nitrogen, Mg. for Each 100 Cc. | Chloride, Mg. for Each 100 Cc. | | |
| 1/13 | 9:00 a. m. | 55.5 | 10.10 | 638 | Preoperative | |
| 1/13 | 3:50 p. m. | 69.3 | 14.00 | 618 | Injected 25 cc. 0.9 per cent sodium chloride for each kilogram | |
| 1/14 | 9:00 a. m. | 71.9 | 14.14 | 627 | Injected 25 cc. 0.9 per cent sodium chloride for each kilogram at 9:00, 1:30 and 4:00 | |
| 1/14 | 4:00 p. m. | 74.8 | 12.82 | 600 | | |
| 1/15 | 2:30 p. m. | 56.5 | 10.28 | 627 | 9:00 and 2:30, same injection; 4:30 injected same amount 0.6 per cent sodium chloride | |
| 1/16 | 3:30 p. m. | 50.5 | 11.42 | 613 | 9:00 and 3:30, injection of 0.6 per cent sodium chloride | |
| 1/17 | 9:00 a. m. | 91.4 | 14.61 | 592 | 9:00, injected 0.6 per cent; 3:30, injected 0.9 per cent | |
| 1/18 | | | | ... | 9:30, injected 0.9 per cent | |
| 1/19 | 9:30 a. m. | 56.5 | 18.18 | 599 | 9:30, 2:30 and 4:30, injected 0.9 per cent sodium chloride | |
| 1/20 | 9:00 a. m. | 82.6 | 14.70 | 635 | 9:00, injected 0.9 per cent sodium chloride | |
| 1/20 | 2:50 p. m. | 82.6 | 9.90 | 658 | 600 cc. of water in rectum | |
| 1/21 | 4:15 p. m. | 84.5 | 14.92 | 579 | 400 cc. of water in rectum | |
| 1/22 | 2:45 p. m. | 90.5 | 16.80 | 519 | 400 cc. of water in rectum | |
| 1/23 | 2:30 p. m. | 86.5 | 25.15 | 566 | 500 cc. of water in rectum | |
| 1/24 | 10:00 a. m. | 94.2 | 21.62 | 486 | Injected 25 cc. 0.9 per cent sodium chloride for each kilogram | |
| 1/26 | 2:00 p. m. | 110.4 | 43.47 | 412 | 200 cc. of water in rectum | |
| 1/27 | 9:45 a. m. | 111.6 | 27.10 | 453 | Gastro-enterostomy performed | |
| 1/27 | 3:00 p. m. | 116.8 | 22.47 | 486 | | |
| Fistulous Fluid and Urine | | | | | | |
| Date, 1925 | Specimen | Volume, Cc. | Period of Collection of Sample, Hours | Urea Nitrogen, Mg. for Total Period | Ammonia Nitrogen, Mg. for Total Period | Chloride, Mg. for Total Period |
| 1/14..... | 1 | 1,000 | 20 | 2,707 | 143 | 4,620 |
| 1/15..... | 2 | 1,200 | 24 | 2,570 | 155 | 6,550 |
| 1/16..... | 3 | 500 | 24 | 150 | 290 | 6,100 |
| 1/19..... | 4 | 1,600 | 72 | 8,792 | 5,168 | 7,648 |
| 1/21..... | 5 | 750 | 12 | 2,400 | 2,700 | 3,397 |
| 1/22..... | 6 | 500 | 20 | 1,700 | 500 | 2,400 |
| 1/23..... | 7 | 1,250 | 24 | 2,500 | 2,000 | 3,287 |
| 1/24..... | 8 | 500 | 20 | 494 | 114 | 625 |
| 1/27..... | 9 | 1,200 | 72 | 1,550 | 2,210 | 1,500 |

The injection of a hypertonic solution of sodium chloride (5 per cent) maintained the chloride content at normal or slightly above, and also prevented a great rise in the urea content of the blood as well as the development of the typical conditions of alkalosis. The life of the animal was not prolonged, but even appeared to be somewhat shortened by the injection of this solution. The injection of hypertonic glucose solution (20 per cent) also failed to prolong the life of the animals, and did not alter the usual chemical changes in the blood.

EFFECTS OF TOTAL AND PARTIAL GASTRECTOMY

Total gastrectomy was performed on certain dogs, the esophageal and duodenal stumps being inverted as blind ends, and partial gastrectomy with gastrostomy on others. In the latter group practically the whole stomach was removed with the exception of a tube 20 cm. in length and 2 cm. in diameter. In the animals with total gastrectomy with

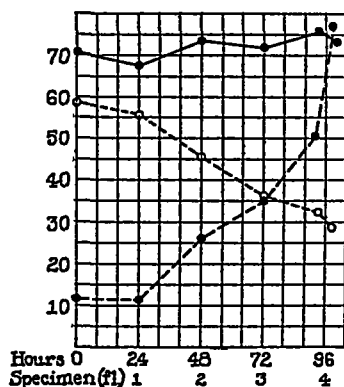


Chart 3.—Chemical changes in the blood in dog following total gastrectomy: solid dot solid line, carbon dioxide; solid dot broken line, urea; open dot broken line, chlorides.

TABLE 3.—Chemical Changes in Blood and Urine of Dog with Total Gastrectomy (Water by Rectum)

| Date, 1925 | | Hours Following Operation | Blood | | |
|------------|--|---------------------------------|--|---|--------------------------------------|
| | | | Carbon Dioxide, per Cent by Volume | Urea Nitrogen, Mg. for Each 100 Cc. | Chloride, Mg. for Each 100 Cc. |
| 1/27..... | | 0 | 71.9 | 12.43 | 591 |
| 1/28..... | | 24 | 68.1 | 12.34 | 556 |
| 1/29..... | | 48 | 74.8 | 26.66 | 462 |
| 1/30..... | | 72 | 73.9 | 36.36 | 369 |
| 1/31..... | | 88 | 76.8 | 51.60 | 330 |
| 1/31..... | | 97 | 74.8 | 77.66 | 297 |

| Date, 1925 | | Specimen | Volume, Cc. | Urine* | | |
|------------|---|----------|----------------|--|--|---|
| | | | | Period of Collection of Sample, Hours | Urea Nitrogen, Mg. for Total Period | Ammonia Nitrogen, Mg. for Total Period |
| 1/28..... | 1 | 500 | 24 | 130. | 10 | 2,405 |
| 1/29..... | 2 | 950 | 24 | 5,341 | 694 | 3,401 |
| 1/30..... | 3 | 1,000 | 24 | 3,510 | 3,530 | 3,490 |
| 1/31..... | 4 | 1,000 | 24 | 2,110 | 2,890 | 2,590 |

* Total fluids collected in metabolism cage.

inverted esophageal and duodenal ends, little change in the carbon dioxide combining power was noted for a period of four days (chart 3, table 3), thus further substantiating the hypothesis that the alkalosis or increase in the carbon dioxide combining power of the blood results from the loss of unneutralized acid through the gastric fistula. Again, in Dog H876 (chart 4, table 4) on whom partial gastrectomy with gastrostomy was performed as described and who received only water by rectum,

there was a rise in the carbon dioxide combining power of the blood plasma of only approximately 14 per cent by volume over a period of four days, a drop of the plasma chloride from 0.615 to 0.420, and but a moderate rise in the blood urea.

It would appear that the retention of alkali by animals with acute gastric fistula is quite similar to the milder degree of alkalosis that occurs in normal animals following the ingestion of food. The forma-

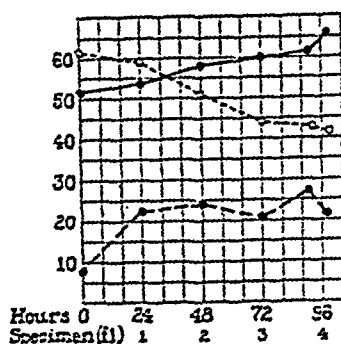


Chart 4.—Chemical changes in the blood in dog with gastric fistula following partial gastrectomy: solid dot solid line, carbon dioxide; solid dot broken line, urea; open dot broken line, chlorides.

TABLE 4.—Chemical Changes in Blood, Urine and Fistulous Fluid of Dog with Partial Gastrectomy and Gastric Fistula (Water by Rectum)

| Date, 1925 | Hours Following Operation | Blood | | |
|------------|---------------------------|------------------------------------|-------------------------------------|--------------------------------|
| | | Carbon Dioxide, per Cent by Volume | Urea Nitrogen, Mg. for Each 100 Cc. | Chloride, Mg. for Each 100 Cc. |
| 1/27..... | 0 | 31.6 | 7.50 | 615 |
| 1/28..... | 24 | 53.6 | 22.72 | 534 |
| 1/29..... | 48 | 53.1 | 21.27 | 513 |
| 1/30..... | 72 | 60.3 | 21.27 | 445 |
| 1/31..... | 91 | 61.3 | 26.06 | 422 |
| 1/31..... | 98 | 65.2 | 21.27 | 430 |

| Urine and Fistulous Fluid | | | | | | |
|---------------------------|----------|-------------|---------------------------------------|-------------------------------------|--|--------------------------------|
| Date, 1925 | Specimen | Volume, Cc. | Period of Collection of Sample, Hours | Urea Nitrogen, Mg. for Total Period | Ammonia Nitrogen, Mg. for Total Period | Chloride, Mg. for Total Period |
| 1/28..... | 1 | 130 | 24 | 411.6 | 105.0 | 651.0 |
| 1/29..... | 2 | 250 | 24 | 1,752.9 | 161.0 | 255.0 |
| 1/30..... | 3 | 500 | 24 | 2,165.0 | 1,315.0 | 1,290.0 |
| 1/31..... | 4 | 600 | 24 | 2,514.0 | 870.0 | 1,550.0 |

tion of acid gastric juice from neutral compounds gives rise to the liberation of equal amounts of alkali which are retained in the body or excreted in the urine. However, even the most active digestive processes produce only a slight alkalosis as compared to that caused by gastric fistula. One might assume from this that the secretion of gastric juice is increased in animals with complete gastric fistula. Certainly there is an exceptional alkali retention in cases of gastric fistula which may be minimized by removal of the stomach or by loss of alkali from the intestine as in duodenal fistula.

In one experiment (chart 3, table 3) following complete gastrectomy with closure and inversion of the esophageal and duodenal stumps the concentration of the blood chlorides reached a minimal level of 297 mg. for each hundred cubic centimeters four days after operation, which would lead to the hypothesis that the reduction in blood chlorides is dependent on a mechanism other than the excretion by the stomach of the chlorine ion. It should be noted that 11.8 Gm. of chlorides were obtained in the fluid passed by rectum and in the urine of this animal during the postoperative life, evidence, we believe, that the reduction of blood chlorides may occur not only from the loss of secretion through the fistula but also as a result of their excretion into the lumen of the intestinal tract.

A study of the urea nitrogen content as well as the ammonia content of the fluids discharged from the gastric fistula and in the urine showed in general that with the increase in the blood nitrogen a similar increase in the nitrogen excreted in the urine and the fluids from the fistula frequently occurred. Immediately prior to death, the nitrogen lost in the fistulous fluids and urine suddenly decreased to a considerable extent, the result, we feel, of impending anuria and may be accounted for as a terminal event. It seemed reasonable that the increase in nitrogen was a result of its increased production. The cause of this increase in the production of urea is by no means certain, but since the oxidation of protein produces an acid residue it may be that the body is employing this means to neutralize the increasing amount of alkali in the tissues. This increase in the production of urea is less marked in those animals with less alkalosis, as is shown by the difference in urea formation in animals with gastric fistula and those with duodenal fistula. However, it should be pointed out that this increase in urea production is not prevented by the administration of salts other than sodium chloride.

In the dogs who had total gastrectomy with inverted esophageal and duodenal stumps (table 3) and also in the ones who had partial gastrectomy with gastrostomy (table 4), the amount of chlorides lost in the fluids of the fistula and urine was as much as, if not more than, that in the dogs who had gastric fistula with the stomach intact (table 1). This appears to be further evidence that the reduction in blood chlorides may occur not only from their loss in the gastric secretion through a fistula, but also as a result of their excretion into the lumen of the intestinal tract. The hypothesis of Haden and Orr¹⁰ is that the loss of blood chlorides is due to their being given up to counteract the effects of toxemia resulting from interference in the motility of the gastrointestinal tract (chart 5).

10. Haden, R. L., and Orr, T. G.: Chemical Changes in the Blood of Man After Acute Intestinal Obstruction, *Surg. Gynec. & Obst.* **37**:465-468 (Oct.) 1923.

SUMMARY

Studies of complete acute gastric fistula in dogs have thrown light on several points. The chemical changes in the blood that occur are quite similar to those occurring in acute duodenal fistula and in high intestinal stasis. There is a marked increase in the carbon dioxide combining power of the blood plasma, an increase in the urea content of the blood, and a decrease in the chloride content. This increase in the carbon dioxide combining power of the blood plasma is much greater than that which occurs in the other conditions mentioned. Similar conditions, in the absence of the stomach or of the greater portion of the stomach, are attended by similar changes, with the exception that the

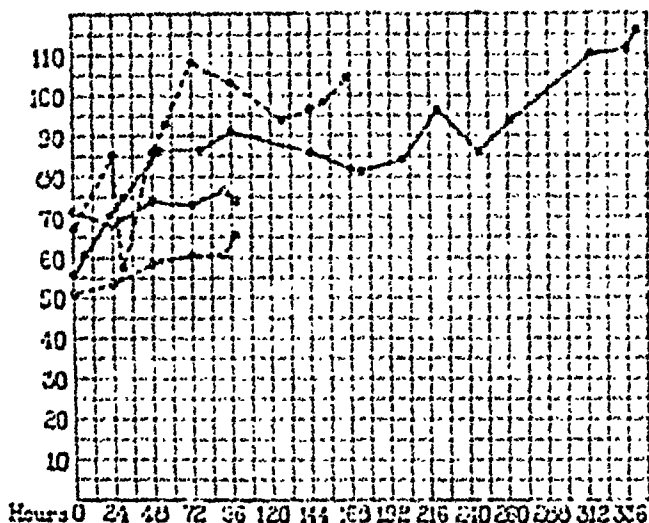


Chart 5.—Comparison of changes in carbon dioxide combining power of the blood in dogs under different conditions: open dot broken line, partial gastrectomy with gastric fistula; open dot solid line, total gastrectomy; solid dot solid line, gastric fistula—intravenous physiologic sodium chloride solution; solid dot broken line, gastric fistula—water by rectum.

carbon dioxide combining power of the blood remains within normal limits. These facts would make it appear that the alkalosis resulting from gastric fistula is due to a loss of acid from the stomach.

The administration to animals with gastric fistula of fluids other than physiologic sodium chloride solution serves to minimize the increase in the urea content of the blood but has little if any effect on the alkalosis or decrease in the chloride content of the blood. The administration of physiologic sodium chloride solution, however, tends to prevent any of these chemical changes from taking place and its use may greatly prolong the life of these animals.

POSTOPERATIVE GASEOUS DISTENTION OF THE INTESTINE

AN EXPERIMENTAL AND CLINICAL STUDY *

M. A. McIVER, M.D.
E. B. BENEDICT, M.D.
AND
J. W. CLINE, JR., M.D.
BOSTON

INTRODUCTION

Gaseous distention of the intestine is one of the most frequent complications following the trauma of abdominal operations, peritonitis or other type of injury to the abdominal viscera. It always entails discomfort to the patient and is sometimes a grave danger. The methods advocated in different clinics for its prevention and treatment are so varied in character and often in such striking contradiction to each other that one is forced to the conclusion that there is no general agreement as to the underlying physiologic processes. These processes are complex, and the amount of experimental work bearing directly on them is small. Some of the more fundamental features of the problem are undoubtedly concerned with the disturbances of motor activity of the gastro-intestinal tract, following injury. A clinical classification and discussion of the different types of injury will be found in articles by Murphy,¹ Rost² and others. The studies of Cannon and Murphy³ should also be consulted: their experimental work deals with retarded intestinal mobility following various forms of injury, and they distinguish between direct injury to the local mechanisms in the wall of the intestine and other injuries that cause a reflex disturbance through the splanchnic nerves.

Although much has been written in regard to the motor effects of injury to the gastro-intestinal tract, many points remain obscure, and clinical articles on the subject of gaseous distention have often failed to make clear the fact that paralysis of the intestine does not per se

* From the surgical services, Massachusetts General Hospital, and the Laboratories of Physiology, Harvard Medical School.

* A preliminary note of this work appeared in the *Boston M. & S. J.* 192:217 (Jan. 29) 1925.

1. Murphy, J. B.: *J. A. M. A.* 26:15 (Jan. 4) 1896.

2. Rost, F.: *The Pathological Physiology of Surgical Diseases*, English Translation, Philadelphia, P. Blakiston's Son & Co., 1923, p. 212.

3. Cannon, W. B., and Murphy, F. T.: *Ann. Surg.* 43:512, 1906; *J. A. M. A.* 49:840 (Sept. 7) 1907.

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cause such distention; the actual ballooning out must be brought about by positive pressure of gas within the lumen. The composition, origin and behavior of these gases are thus important features of the problem of distention.

Source of Gases of the Intestinal Tract.—The gases of the intestinal tract were first systematically studied by Plamer⁴ in 1800, and the work was later amplified by Ruge,⁵ Tappeiner,⁶ Tacke,⁷ and others. An extensive bibliography on the subject has been collected by Kantor.⁸ The writers agree that the gases commonly present in intestinal meteorism are carbon dioxide, oxygen, nitrogen, hydrogen, methane and (sometimes) hydrogen sulphide, the proportions being subject to considerable variation. In considering the relation of these gases to distention, their origin must be taken into account.

One well-recognized and important source for certain of the gases is found in the decomposition of intestinal contents. The work of early German writers, already mentioned, and the more recent studies by Boycott and Damant⁹ furnish data on this subject and emphasize the influence of different types of diet on the kind of gas produced.

A second source is found in the diffusion of blood gases into the intestinal lumen. The walls of the intestine are permeable to gases, and an active interchange takes place, tending to keep the gases on the two sides of the intestinal mucosa in equilibrium. The mechanism of this exchange is discussed in detail in a report of our recent studies on the subject.¹⁰

A third, and less acknowledged, source for these intestinal gases must be considered. The gas normally found in the stomach consists primarily of atmospheric air, admitted by swallowing. Under conditions that will be described later, the amount of air is considerably increased, and we have come to believe that its passage downward into the intestine may be an important factor in the production of distention in certain cases. Articles by Ylppö¹¹ and Kantor⁸ refer to this source of gas, and Beckham¹² mentions it as a factor in postoperative distention.

4. Plamer, J.: *Sitzungsber. d. k. Akad. d. Wissensch., Math.-naturw. Cl.* **42**: 307, 1800.

5. Ruge, E.: *Sitzungsber. d. k. Akad. d. Wissensch., Math.-naturw. Cl.* **11**: 739, 1861.

6. Tappeiner, H.: *Ztschr. f. Physiol. Chem.* **6**: 432, 1882.

7. Tacke, H.: *Ueber die Bedeutung der brennbaren Gase im tierischen Organismus*, inaugural dissertation, Berlin, 1834.

8. Kantor, J. L.: *Am. J. M. Sc.* **155**: 829 (June) 1918.

9. Boycott, A. E., and Damant, G. C. C.: *J. Physiol.* **36**: 283, 1907.

10. McIver, M. A.; Redfield, A. C., and Benedict, E. B.: *Am. J. Physiol.* **76**: 92, 1926.

11. Ylppö, A.: *München. med. Wchnschr.* **63**: 1650, 1916.

12. Beckham, W. S.: *Operative Surgery*, Philadelphia, 1924, 1: 317.

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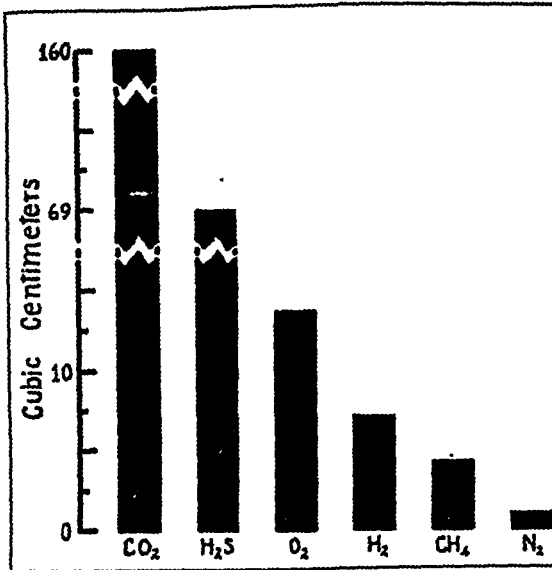
1. Murphy, J. B.: *J. A. M. A.* 26:15 (Jan. 4) 1896.

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In general, however, it has not received much attention in the literature, and little or no direct evidence has existed on which to judge its importance in the distention encountered in surgical practice.

The Body's Method of Eliminating Intestinal Gases.—The expulsion of gas by motor activity of the intestine is an important method of eliminating abnormal accumulations, and as stated above the interference with this mechanism which sometimes follows injury is a cardinal factor in distention. It is not, however, the sole method of eliminating gas. The diffusion of blood gases into the intestinal lumen was mentioned in a preceding paragraph; equally active is the reverse process, namely, the absorption of intestinal gases into the blood stream. Studies were recently carried out on this point by inject-



Relative rates of absorption, expressed in cubic centimeters, of carbon dioxide, hydrogen sulphide, oxygen, hydrogen, methane and nitrogen from a 25 cm. loop of the small intestine of the cat. The height of the columns represents the number of cubic centimeters of the gas absorbed over a period of one hour. In the case of carbon dioxide, because of the rapidity of its disappearance, and of hydrogen sulphide, because of its toxicity, the gas was withdrawn after the lapse of a few minutes, and the rate of absorption for one hour was calculated.

ing known quantities of the several gases into an isolated loop of intestine, leaving the gas for definite periods of time, withdrawing it, and determining the amount of absorption that had taken place. These experiments showed that while the rates of absorption vary greatly for the different gases, the amounts that can be eliminated by this mechanism are considerable. Figure 1, taken from a report¹⁰ of this work, gives the relative rates of absorption of the gases commonly encountered in the intestinal tract. The height of the first column represents the amount of carbon dioxide, a gas liberated in great quantities when

fermentation is active, which can be eliminated in one hour from an isolated intestinal loop 25 cm. long. It is evident that the amount of this gas which could be absorbed in twenty-four hours from the intestine as a whole would be large. The next column represents hydrogen sulphide, a gas that is toxic to the organism, and this also is eliminated rapidly. The other gases represented show a slower rate of absorption; but it is obvious that any of them, with the exception of nitrogen,¹³ could be eliminated in considerable quantities by this mechanism.

The rate of absorption of atmospheric air also was tested in these experiments, although the results are not shown in figure 1, and was found to be low, only 4 cc. being absorbed from a 45 cm. loop in five hours. This is to be expected, because of the close similarity between the composition of atmospheric air and that of the blood gases, and is of importance in connection with the view that air is a source of gas in distention.

Effect of Interference with the Circulation on Elimination of Intestinal Gases.—Since the absorption of intestinal gases by the blood stream is such an important method of elimination, it appears obvious that interference with the splanchnic circulation would upset this process and have serious consequences. It must be remembered, however, that there is little direct evidence where minor degrees of circulatory disturbance exist, and in the literature too much stress has been placed on this explanation for meteorism of obscure origin. The experiments of Kato,¹⁴ who reported a slow absorption of carbon dioxide after ligation of the portal vein, and our own experiments on partial obstruction of this vein, represent too extreme a disturbance of the circulation to afford a useful comparison with clinical conditions, except in types of intestinal obstruction involving gross interference with the blood supply or in cases of thrombosis of the mesenteric veins.

Our experiments showed that if the veins to an empty intestinal loop are ligated, distention of the intestine by a bloody, fluid exudate will follow within a few hours,¹⁵ owing to an increase in capillary

13. When 20 cc. of nitrogen are introduced into an empty intestinal loop, the absorption at the end of six hours is about 7 cc. If the same amount of nitrogen is introduced into an isolated loop in which digestion is in progress, at the end of the six hours the loop will be found greatly distended with gas. This is probably due to the fact that the abnormal presence of gas interferes with digestion and absorption and contributes to an active fermentation. This suggests that a vicious circle may be an important factor in marked degrees of distention, i. e., the presence of gas in an intestine in which digestion is in progress may result in increased fermentation and decreased absorption.

14. Kato, K.: *Internat. Beitr. z. Path. u. Therap. d. Ernährungstör.* 1:315, 1910.

15. Murphy, F. T., and Vincent, B.: *Boston M. & S. J.* 165:684, 1911. Murphy, F. T., and Brooks, Barney: *Intestinal Obstruction, Arch. Int. Med.* 15: 392 (March) 1915.

pressure and damage caused by a poor supply of oxygen. If the intestinal loop is distended with air before the veins are obstructed, in addition to the fluid exudate, the volume of gas will increase, owing to a diffusion into the lumen of carbon dioxide from the blood.

PRESENT STUDIES

In a preceding paragraph, atmospheric air has been mentioned as a source of gas in intestinal distention. In the present studies an attempt has been made to estimate its importance in the distention following injury to the abdominal viscera. The work has consisted of animal experiments, supplemented by certain clinical studies.

Animal Experiments.—In order to determine some of the factors that govern the passage of air from the stomach into the intestine, certain animal experiments were carried out. These consisted of direct observations on the behavior of the stomach inflated with air. Additional experiments were carried out on the rôle of atmospheric air in the distention that accompanies general peritonitis. Abbreviated protocols illustrating salient features are appended.

METHOD

Cats, under chloralose anesthesia, were used in all these experiments. The observations were carried out in a moist chamber devised and described by Veach.¹⁶ This piece of apparatus consists of a copper box large enough to receive a cat extended on an animal board; the bottom of the box contains water, warmed by an electric heating coil; the lid is supplied with glass windows for the purpose of observation, and small apertures permit the insertion of thermometer, tube from the tracheal cannula, etc.

After anesthetization, the animal was placed in the moist chamber, and the abdomen opened, the abdominal walls being held apart by ligatures attached to the sides of the box. From 60 to 90 cc. of air was introduced into the stomach, causing a moderate degree of distention; considerably more than this amount of gas is often encountered in the normal fasting stomach of the cat. In addition to observations on the course of events following this simple inflation of the stomach, the effects on the dilated stomach of stimulation or section of the splanchnic and vagus nerves were noted.

RESULTS

Effects of Simple Distention of the Stomach.—Vigorous peristaltic waves were usually set up following moderate inflation of the stomach. In certain experiments these continued for several hours without the

16. Veach, H. O.: Am. J. Physiol. 71:229 (Jan.) 1925.

passage of gas from the stomach into the intestine; from time to time rhythmic activity of the small intestine and colon was observed. In other experiments, after a short period of gastric activity the small intestine and colon became distended, the stomach decreasing in size as the gas was passed into the lower intestinal tract (experiment 1). If the intestine is obstructed, gas will be passed down from the stomach and accumulate above the point of obstruction, and may there be drawn off (experiment 1). It is thus evident that during moderate distention the stomach is capable of passing gas into the lower intestinal tract.

Effects of Vagus and Splanchnic Section.—The splanchnic nerves were sectioned on the posterior abdominal wall shortly beyond their entrance into the abdominal cavity; the vagi were cut just below their entrance into the abdominal cavity, the dissection being carried around the esophagus down to the muscularis.

Following section of both splanchnic and vagus nerves, the motor activity of the stomach and intestinal tract was increased. Under this condition the gas was invariably passed from the stomach into the intestine. Experiment 2 is typical.

Effects of Vagus Stimulation.—Stimulation of both right and left vagi in the neck was carried out with the stomach distended by gas and resulted in great motor activity of the stomach and small intestine; but in no case was any gas observed to pass from the stomach to the intestine. This result was expected, since the increased tone and the contractions of the pylorus and duodenum would act as barriers to the passage of gas downward.

Effects of Splanchnic Stimulation.—When strong stimulation was applied to the splanchnics, major and minor, of the left side, just beyond their entrance into the abdominal cavity, increased tone in the stomach and an increase in peristaltic waves were noted in a number of cases. Under these conditions gas was passed down into the duodenum (experiment 3). Since this result was not abolished by cutting the splanchnic on the opposite side, and since the same result was obtained when stimulation was applied to the proximal, i. e., the spinal, end of the cut splanchnic, it would appear to be a reflex phenomenon transmitted through the vagi. When stimulation was applied to the distal end of the cut splanchnic (experiment 3), the typical inhibition of the movements of the stomach and intestine and the blanching due to constriction of the blood vessels, which were described by early observers, were noted. In certain cases during the increased activity following the period of inhibition gas was passed down. It is interesting that afferent impulses passing by way of the splanchnics are effective in causing a passage of gas from the stomach into the lower intestinal tract.

Effects of Peritonitis.—In addition to the experiments described above, certain others were carried out in order to determine whether by preventing the entrance of air from the stomach the occurrence of intestinal distention in general peritonitis might be prevented. The abdomen of the cat was opened, under ether anesthesia, and a massive peritoneal infection produced by the injection of a few cubic centimeters of colonic contents into the peritoneal cavity. In three of the six experiments at the time of this injection the pylorus was ligated. The abdomen was then closed. The animals quickly recovered from the immediate effects of the operation, but at the end of twenty-four hours showed systemic effects of the peritoneal infection. After twenty-eight hours, a lethal quantity of a barbituric acid derivative was administered and a necropsy performed.

The results were as follows: All the cats showed evidence of general peritonitis. The stomachs of all were dilated with gas. In the animals with pyloric obstruction, there was no distention of the small or the large intestine. In the animals in which no such obstruction had been produced, the findings were: One showed the stomach and upper 3 feet of small intestine distended; another, the stomach and upper three-quarters of small intestine distended; the third, the stomach and whole length of small intestine dilated. The colon was not dilated in any instance. Experiments 4 and 5 are typical.

These experiments suggest that atmospheric air is an important factor in the distention that accompanies general peritonitis; but they should not, of course, be construed as meaning that air is the sole source of gas. Fermentation of stagnating intestinal contents undoubtedly plays a rôle in most cases, and may at times be the most important source of gas.

CLINICAL STUDIES

The experiments described in the foregoing show that under certain conditions gas is passed down from the stomach to the intestine, and suggest that this may be one mechanism of intestinal distention. In order to see if any clinical confirmation of this view could be obtained, the following studies were carried out.

Gas Analyses from Postoperative Cases.—The first aspect taken up was the composition of the gases responsible for the distention encountered after operation. In table 1, analyses of gases from the patients in the surgical wards showing postoperative distention are presented, with additional analyses from distended cases in the medical wards for comparison. The data are not sufficiently complete to warrant detailed discussion; but attention is drawn to several points.

The gases found are the same as those identified by previous workers. In one instance only was hydrogen sulphide found to be present; it is

TABLE 1.—Gas Analyses from Distended Patients in Surgical and in Medical Wards *

| Date | Diagnosis and Operation | Diet | Analysis of Gas | | | | | | Postoperative patients in surgical wards |
|------|--|-------------------------------------|-----------------|--------|----------|---------|-------------------|----------|--|
| | | | Carbon Dioxide | Oxygen | Nitrogen | Methane | Hydrogen Sulphide | Hydrogen | |
| 3/11 | Cholelithiasis (cholecystectomy) | Soft solids | 4.0 | 4.2 | 83.0 | 1.7 | 2.1 | .. | Patients in medical wards |
| 3/12 | Cholelithiasis (cholecystectomy) | Liquids and soft solids | 3.8 | 9.4 | 88.6 | 2.2 | 0.0 | .. | |
| 3/12 | Retroversion of uterus (suspension and appendectomy) | Liquids | 5.8 | 1.6 | 91.5 | 1.1 | 0.0 | .. | Patients in medical wards |
| 4/9 | Ventral hernia (repair of hernia) | Soft solids, but ate almost nothing | 6.2 | 0.0 | 90.1 | 2.4 | 1.3 | .. | |
| 5/20 | Cholelithiasis (cholecystectomy) | Low residue | 8.5 | 1.8 | 84.7 | 17.9 | 2.5 | .. | Patients in medical wards |
| 2/18 | Pneumonia | Soft solids | 11.8 | 1.7 | 66.1 | 8.7 | 3.2 | .. | |
| 2/20 | Pneumonia | Chiefly milk | 5.4 | 2.0 | 80.7 | 3.3 | 33.1 | .. | Patients in medical wards |
| 2/19 | Cardiac decompensation | Chiefly milk | 7.5 | 1.3 | 51.8 | 6.1 | 24.6 | .. | |
| 2/25 | Cardiac decompensation | Chiefly milk | 14.0 | 0.9 | 55.3 | 5.3 | 34.3 | .. | Patients in medical wards |
| 2/27 | Cardiac decompensation | Soft solids, with milk | 9.6 | 1.4 | 49.2 | 19.4 | 6.5 | .. | |
| 2/25 | Diverticulitis | Soft solids | 11.6 | 0.0 | 62.5 | 0.0 | 5.2 | .. | Patients in medical wards |
| 2/20 | Diarrhea | Milk and toast | 10.5 | 2.2 | 82.1 | 0.0 | 5.2 | .. | |
| 3/12 | For study | | 5.1 | 1.1 | 89.1 | 1.3 | 3.4 | .. | |

* The gases were collected under paraffin oil in a glass cylinder, by means of a rectal tube and a connecting tube which were also filled with oil. The gases were analyzed on a Haldane gas analyzer equipped with a combustion chamber. Lead acetate paper was used in testing for hydrogen sulphide.

probably rarely formed in large quantities and its absorption is rapid, as may be seen in the accompanying chart. The percentages of carbon dioxide, with a few exceptions, are close to those in venous blood, which is not surprising since this gas has a rapid rate of diffusion and is readily soluble in blood. The percentages of nitrogen are uniformly high, and since free nitrogen is liberated in the intestine only in small quantities if at all,¹⁷ it must be derived from air: either directly, from swallowed air, or indirectly, by diffusion from the blood stream, which is saturated with nitrogen at four-fifths of an atmosphere of pressure. The oxygen figures are uniformly low. This probably means that the tension of this gas is low in the capillaries of the colon during distention, although a certain amount is used up in the process of fermentation. The percentages of hydrogen and methane are lower in the patients showing postoperative distention than in the medical cases, which suggests that fermentation was less active in the former; and since the composition (except for the small amounts of hydrogen and methane) is that of air modified by interchange with the blood gases, the findings are not inconsistent with the view that swallowed air plays a rôle in the production of postoperative distention.

Incidence of Gaseous Distention.—In order to form a basis for studies on the importance of atmospheric air in postoperative distention, an attempt was made to estimate the frequency with which this complication is encountered following abdominal operations. Very little information was found in the literature on this point (except in the work of Martzloff,¹⁸ who discusses distention in relation to certain preoperative medication and will be referred to later) or as to the relative frequency following different types of surgical procedure. A study was therefore made of 107 cases in which a laparotomy had been performed. The classification of these cases, shown in table 2, is based on the anatomic site of the operation. Perhaps a more logical grouping would take into account the amount of trauma occasioned by the different operations and the degree of peritonitis present; but these points are so difficult to evaluate that it seemed safer to discuss the cases on a regional basis.

To determine the presence or absence of moderate degrees of distention is not an easy matter. The method used in making the present study was as follows: Immediately after operation, the appearance of the abdomen was noted and the circumference measured with a tape. For three or four days following the operation, longer if distention persisted, the patient was visited daily. It was found impossible to place great reliance on the measurements alone, especially when the changes

17. Krogh, A.: *Skandin. Arch. f. Physiol.* 18:364, 1906.

18. Martzloff, K. H.: *Bull. Johns Hopkins Hosp.* 35:370 (Nov.) 1924.

were slight; at the daily visits, therefore, in addition to the measurements the whole picture was taken into consideration: the appearance of the abdomen, the amount of tympany, etc. The results are given in table 2.

Of the 107 patients followed, thirty-six were considered to suffer from distention, although inevitably in a number of instances there might have been a difference of opinion by other observers, since in only a few cases was the distention severe. As will be noted, the patients who had undergone operations on the biliary tract showed the highest incidence of distention. The next highest incidence was found in the "pelvic cases," a group representing operations on the uterus and adnexa. The gastro-intestinal cases come next: a varied group involving operations on the stomach and duodenum, removal of the appendix, and so forth. The fourth or "miscellaneous" group consists chiefly of exploratory operations and operations on the kidney. Since hernia operations involve localized trauma to the peritoneum, twenty-nine patients were followed after operation; only one was distended.

TABLE 2.—*Classification in One Hundred and Seven Laparotomy Cases*

| Biliary | Pelvic | Gastro-Intestinal | Miscellaneous |
|------------------|-------------------|-------------------|------------------|
| Total.....25 | Total.....34 | Total.....34 | Total.....14 |
| Distended.....12 | Distended.....13 | Distended..... 8 | Distended..... 3 |
| | Total.....107 | | |
| | Distended..... 36 | | |

Additional Observations.—In addition to making the observations described above concerning distention, certain other points were noted, which for the sake of clearness were not included in table 2 but will now be briefly commented on.

The anesthetic employed, except in a few cases, was ether, preceded as a rule by nitrous oxide. The length of operation did not apparently influence the incidence of distention. In the majority of the cases the distention was apparent at the end of twenty-four hours. This agrees in general with the findings of Martzloff.¹⁸ The usual duration was from forty-eight to seventy-two hours.

The subjective sensations of the patients also were recorded. The most important of these consisted of intermittent, shifting, cramplike pains which are usually referred to as "gas pains" but which do not necessarily imply any appreciable degree of gaseous distention. While most of our patients complaining of these pains did have a measurable distention of the abdomen, a number showed no visible evidence. About 50 per cent, for instance, of the patients of the first group shown in table 2 complained of "gas pains," and about the same percentage of the second group in table 3, although the incidence of distention was much

lower in the latter group. It is well known, also, that in the graver forms of distention, such as often accompany general peritonitis, while the patients may feel discomfort from distention, they do not suffer from "gas pains." It seems reasonable to suppose that this type of discomfort represents abnormal peristaltic activity of the intestinal tract, which, although usually associated with gas, may take place independently of any distention of the intestinal lumen.

Dilatation of the Stomach Following Operations.—Postoperative dilatation of the stomach is not uncommon. Leaving out of consideration the etiology of the most extreme form of this condition, known as acute dilatation, we find a number of causes for the presence of an unusual amount of air in the stomach after operation. It is, for example, well known that a great deal of air may be swallowed during the early stages of anesthetization: in three of the cases observed, 115, sixty-seven and fifty-four swallowing movements, respectively, were noted while the patients were being etherized. Again, it is a matter of common observation that great dryness of the mucous membrane of the mouth and pharynx is one of the after-effects of ether, and that many patients make an effort to relieve this by swallowing motions which carry air into the stomach. It was also observed that many of our patients following operation complained of gas in the stomach, which they often attempted to relieve by belching, and undoubtedly more air was swallowed in an attempt to relieve the gastric distress. A certain amount of air, also, is carried into the stomach at each swallowing motion when liquids are taken, and the exclusively liquid diet given after operation must be responsible for a considerable intake of air. It is also possible that during the retching which accompanies nausea and vomiting air may be gulped down.

Experiments with the Stomach Tube.—It has already been suggested that the air which is present in the stomach in unusual quantities after operation may be passed into the intestine and play an important part in intestinal distention. If this were true, it would seem possible that the incidence of this condition might be lessened by preventing the accumulation of air in the stomach. This supposition was tested in the following manner: While the patient was still under ether, a small stomach tube of the type advocated by Levin¹⁹ was passed into the stomach through the nares. The gaseous contents of the stomach were then drawn off by means of a syringe; the tube was left in position for from twenty-four to forty-eight hours, and the gastric contents aspirated twice daily. The average amount of gas drawn off at the first aspiration was 145 cc.; the largest amount, 600 cc. In certain cases, in addi-

19. Levin, A. L.: J. A. M. A. 76:1007 (April 9) 1921.

tion to the gas present there was an accumulation of fluid, the largest amount found being 480 cc., the usual amount much less.

In the group of cases in which this procedure was carried out, the incidence of distention was considerably reduced, as will be noted in table 3 in contrast to the group of cases shown in table 2 in which the procedure was not followed.

While the group thus tested was small, the more serious types of cases only were included, and the fact that the incidence of distention is low offers suggestive evidence that the passage of air from the stomach to the intestines does play an important part in the production of postoperative distention. Several clinical observations might be considered as in accordance with this idea. Was this mechanism, for example, in part responsible for the failure in preventing distention of the old preoperative regimen which included dietary restrictions and a free use of strong cathartics? Interesting, also, in this connection is the

TABLE 3.—Cases in Which Stomach Tube Was Used

| Biliary | Pelvic | Gastro-Intestinal |
|------------------|------------------|-------------------|
| Total.....11 | Total..... 8 | Total..... 6 |
| Distended..... 2 | Distended..... 0 | Distended..... 1 |
| | Total.....25 | |
| | Distended..... 3 | |

effect of morphine after abdominal operations, for if fermentation due to inhibited motor activity of the intestine were the only source of gas, it might appear illogical to give a drug that would further inhibit peristalsis, and yet morphine is used liberally after abdominal operations and in the treatment of peritonitis, and the claim is made in many clinics that it has a tendency to prevent distention. (A census of clinics with reference to the use of morphine after operation has recently been made by Slocum²⁰.) Its beneficial effect may be explained in various ways, some of which will be touched on later; but among others it is suggested that by relieving gastric distress and diminishing reflex actions in general, morphine lessens the tendency to take air into the stomach, and by quieting gastric peristalsis it decreases the passage of air from the stomach into the intestine. It is also possible that the absorption of gas proceeds most rapidly from a quiet intestine.

TREATMENT

Certain points concerning treatment, some of them suggested by the foregoing studies, will be briefly discussed.

As regards the preoperative management of a case, the guiding principle should be to avoid as far as possible procedures that interfere

20. Slocum, M. A.: J. A. M. A. 84:1264 (April 25) 1925.

with the normal functions of the intestine, and it should be remembered that this applies not only to the motor function but also to the absorbing function. It is obviously an advantage to have the stomach and small intestine empty and at rest at the time of operation; but a long starvation period is not necessary, since according to Alvarez²¹ it requires only from seven to nine hours under normal conditions for the stomach and small intestine to become empty after a meal. In order that fermentation in the large intestine may be reduced to a minimum, it would seem logical to give a low residue diet during the day preceding operation. With the idea of further reducing fermentation in the colon, an enema on the morning of operation is frequently prescribed. Unless there is some special indication for this procedure, however, its wisdom may be open to question, for an important function of the colon is the dehydration of the contents received from the small intestine, and an enema often leaves a great deal of liquid feces which may result in more fermentation than if the normal condition had not been disturbed. The use of violent cathartics has been so universally abandoned that it does not seem necessary to touch further on this point; articles by Peet²² and Alvarez and Taylor²³ cover the subject from both clinical and experimental points of view.

In the treatment after operation, one must of course be governed by the exigencies of the case; but it should be emphasized at this point that since rest is a fundamental principle in the treatment of injury, morphine, by quieting intestinal movements and preventing the spread of infection, provides the conditions most favorable for the recovery of the gastro-intestinal tract from the trauma of operation or other type of injury; and the relief from pain which it furnishes must be beneficial to the organism as a whole. Other modes of action by which morphine may prevent or relieve distention have already been suggested.

Consistent with the use of morphine to quiet intestinal movement is the policy at this clinic to avoid drugs such as pituitary extract and physostigmine, which are capable of setting up violent types of peristalsis. There may be occasional circumstances in which they are of use, and the arguments in their favor will be found in articles by Craig²⁴ and Martin and Weiss,²⁵ and also by Cross,²⁶ who has advocated a combination of the two. It is, however, interesting to note in this con-

21. Alvarez, W. C.: *Surg. Gynec. Obst.* 26:651 (June) 1918.

22. Peet, M. M.: *J. A. M. A.* 71:175 (July 20) 1918.

23. Alvarez, W. C., and Taylor, F. B.: *J. Pharmacol. & Exper. Therap.* 10 365 (Nov.) 1917.

24. Craig, D. H.: *New York M. J.* 81:527, 1905.

25. Martin, H. E., and Weiss, S.: *Use of Physostigmine in Abdominal Distention*, *J. A. M. A.* 84:1407 (May 9) 1925.

26. Cross, D. G. T. K.: *Brit. M. J.* 1:9 (Jan. 5) 1924.

nection that according to Martzloff,¹⁸ in cases in which physostigmine (eserine) and strychnine were given before operation there was a higher incidence of distention than in those cases in which this treatment was not administered.

In the presence of distention of the colon, enemas often give relief. It is questionable whether their use should be pushed if they do not seem to produce this result. Hot applications to the abdomen, such as turpentine stupes or flaxseed poultices, especially when combined with the rectal tube, are unquestionably an important method of treating distention; it is probable, although there is no experimental evidence to support this view, that they stimulate a gentle, effective peristaltic action without setting up areas of localized contractions; and they may, perhaps, relax such contracted areas when these exist. It is also possible that they favor the absorption of gases from the intestine.

When we consider the influence of the postoperative diet, certain points might be mentioned. It is a generally accepted custom to use a liquid diet for a few days following abdominal operations. A theoretical objection might be raised to the use of milk during the period when distention is likely to occur, since it has been shown by the work of Ruge⁵ that in the fermentation of milk a high percentage of hydrogen, a gas that is absorbed slowly, is liberated. As soon as circumstances permit, an ordinary diet should be resumed, since the intestine probably functions to best advantage under those conditions.

Our series of experiments showed that the small type of stomach tube, left in place for from twenty-four to forty-eight hours after operation, was of definite benefit in preventing distention. In the majority of instances the tube caused little or no discomfort to the patient and did not interfere in any way with the taking of nourishment. Since it is occasionally a source of annoyance to the patient, its use indiscriminately is not advocated; but in certain cases in which distention is feared as a grave complication it should be employed.

SUMMARY

1. The origin of the gases found in intestinal meteorism is threefold: the decomposition of intestinal contents; the diffusion of blood gases into the intestinal lumen through the mucosa, and the passage of atmospheric air from the stomach into the intestine. Absorption into the blood stream is an important method of eliminating intestinal gases. The rate at which absorption proceeds varies greatly for the different gases (discussed in text). The absorption of atmospheric air is slow, because of its similarity in composition to the blood gases, a point of importance in relation to air as a source of gas in distention.

2. Animal experiments showed that gas may be forced from the stomach into the lower intestinal tract by peristalsis or by increased gastric tone, thereby causing distention of the small intestine and colon. The increased motor activity from moderate distention of the stomach is at times sufficient to bring this about. Section of the extrinsic nerves (vagus and splanchnic) invariably resulted in increased activity and the passage of air downward. Afferent impulses by way of the splanchnics are also capable of producing this result.

The experiments on the distention accompanying general peritonitis suggest that atmospheric air is an important source of gas in these cases.

3. The validity of the supposition that air might be passed down from the stomach to the intestine, causing postoperative distention, was tested by preventing accumulations of air in the stomach through the use of the stomach tube. By this means the incidence of distention was considerably reduced, as shown in tables 2 and 3, suggesting that air may be an important source of gas in postoperative intestinal distention. Gas analyses from cases showing postoperative distention were consistent with this view.

4. Since rest is a fundamental principle in the treatment of injury, the quieting effect of morphine is beneficial and drugs such as physostigmine or pituitary extract which are capable of setting up violent types of peristalsis should usually be avoided. In cases in which serious distention is feared, the continuous use of a small stomach tube during the critical period should be considered.

PROTOCOLS

EXPERIMENT 1.—November 20; male cat; weight, 2 Kg. A small amount of milk was given the preceding night.

11:00: animal etherized; 9.5 cc. of chloralose given intravenously.

1:15: animal placed in moist chamber; abdomen opened. The stomach contained a small amount of gas; the small intestine and colon appeared flat. Peristaltic waves were noted over the stomach and coils of the small intestine.

1:30: 60 cc. of air introduced into stomach by syringe and needle.

2:10: dilatation of upper coils of small intestine noted; stomach appeared somewhat smaller.

2:25: stomach markedly decreased in size.

2:30: colon, which had been almost invisible, became dilated. Needle introduced and 30 cc. of gas drawn off from stomach, completely emptying it.

2:40: the gas was milked out of upper part of small intestine, and a needle with rubber tube attached was inserted about 30 cm. from pylorus and held in place by a silk ligature around the intestine. The rubber tube, previously filled with water, was carried under a test tube filled with water and immersed in a beaker of water. Ninety cubic centimeters of air was introduced into stomach; complete inhibition of all movements of stomach and intestine followed.

4:27: peristaltic waves again noted passing over pyloric portion of stomach.

4:55: peristalsis very active over stomach and upper part of small intestine. Small intestine appeared gas-containing, gas being pushed by peristalsis almost to the point of obstruction.

5:10: gas bubbled through needle and rubber tubing and was collected in the test tube under water.

EXPERIMENT 2.—November 22; female cat; weight, 2.2 Kg. No food for twenty-four hours.,

9:50: light ether; 12 cc. of chloralose injected intravenously.

11:30: animal placed in moist chamber; abdomen opened. Stomach small in size; small intestine and colon collapsed. Vigorous peristalsis over stomach and in certain coils of small intestine.

11:35: 60 cc. of air introduced into stomach.

12:05: deep waves passing over stomach, but no gas has entered duodenum.

12:15-12:24: right and left splanchnics, major and minor, divided. Vigorous peristalsis noted over small intestine and stomach. Moderately deep waves over cardiac portion, but this did not extend down over the antrum pylorus. While tone over stomach appeared marked, peristaltic waves were disordered and passed over stomach in disorderly fashion, making it appear as though the gas were being churned up and down. No gas was discharged into small intestine.

12:50: right and left vagi cut, just above cardia.

1:00: deep peristaltic waves passing over entire stomach at rate of 8 per minute.

1:10: duodenum dilated.

2:30: duodenum and upper coils of small intestine distended with gas.

EXPERIMENT 3.—January 12; female cat; weight, 2 Kg. No food for twenty-four hours.

10:20: ether started; 8 cc. of chloralose given intravenously.

11:00: light ether, while tracheal cannula was inserted.

12:00: animal light; additional 2 cc. of chloralose given.

12:45: animal placed in moist chamber. Abdomen opened.

1:00: left splanchnics, major and minor, isolated, and guarded electrode, connected with an inductorium, applied to the nerves.

1:15: moderately strong stimulation applied for one and one-half minutes. Great blanching of blood vessels of stomach and intestine noted. Tonus rings appeared over pyloric portion of stomach, but no air descended.

1:20: irregular peristaltic waves observed over cardiac portion of stomach.

1:25: splanchnic stimulated for one and one-half minutes. Great increase in stomach tone, with deep peristaltic waves. Air forced into duodenum during and following this stimulation.

2:45: left splanchnic divided, between ligatures.

3:00: stimulation of distal end of cut splanchnic for one minute. Blanching of blood vessels and inhibition of stomach activity noted. Return of gastric activity a few minutes after stimulation stopped. During this time a small amount of air entered duodenum.

3:25: electrodes applied to proximal end of cut splanchnic.

3:27: stimulation for one minute.

3:30: right splanchnic cut.

3:45: stimulation of proximal (spinal) end of left splanchnic. Increase in gastric tone and deep tonus waves noted. Duodenum distended by gas which was observed entering from the stomach.

EXPERIMENT 4.—June 16; weight, 3.5 Kg. Had access to water, but no food for twenty-four hours.

Abdomen opened under ether anesthesia; stomach contained usual amount of air (estimated 50 cc.); small intestine and colon flat.

Portion of omentum resected. A needle introduced into the colon and about 1 cc. of semifluid material drawn into syringe. Diluted with water to 5 cc. and injected into peritoneal cavity.

June 17: cat listless, not inclined to move about.

June 18: cat looked sick and listless, and had vomited several times. A lethal dose of a barbituric acid derivative was administered.

Necropsy: abdomen opened; purulent peritonitis present. Stomach dilated with gas; upper three-fourths of small intestine distended with gas; colon flat.

EXPERIMENT 5.—June 16; weight, 2.3 Kg. Had access to water but no food for twenty-four hours.

Abdomen opened under ether anesthesia; stomach and intestine empty. A portion of omentum resected and peritoneal cavity infected as in preceding experiment.

Pylorus ligated.

June 17: general appearance indicated severe infection; had vomited once.

June 18: general condition appeared worse; very drowsy and listless. A lethal dose of a barbituric acid derivative was administered.

Necropsy showed purulent peritonitis. Stomach greatly dilated with gas. Small intestine empty except for a small amount of bile stained fluid. Colon empty.

THIRTIETH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY *

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(Concluded from page 458)

PERIPHERAL NERVE SURGERY

Nerve Anastomosis.—Ballance, Colledge and Bailey³² have made an experimental study of various methods of nerve anastomosis. They conclude that with sutures of absorbable material it is unimportant whether the suture passes through the neurolemma alone or whether it penetrates the nerve substance. Varnishes were tried as a substitute for sutures, but the only one that was at all successful was that made by cutting a piece of living muscle into fine bits and pounding this up with a few drops of salt solution in a mortar so that sarcous material was set free. Anastomosis by the method of double lateral implantation was successful if the ends were placed not too far apart. When a median incision is made in the receiving nerve the tendency is for the two ends to become connected. Exact end-to-end suture of the nerve fibers is not possible in any case.

Traumatic Neuritis of the Ulnar Nerve.—Platt³³ has made a thorough study of the pathogenesis and treatment of traumatic neuritis of the ulnar nerve in the postcondylar groove of the humerus. He points out that normally the nerve is mobile in this situation and may even be hypermobile. The condition is discussed under three headings: first, fracture of the lower end of the humerus with early involvement; second, late involvement; third, recurring dislocation of the nerve from its bed. Of 329 cases of fracture of the region of the elbow treated by Platt, involvement of the ulnar nerve was encountered in only nine cases. All of these occurred in fractures of the humerus and eight were in fractures of the internal condyle. Seven of these patients recovered spontaneously in from three to eight months. In 600 operations on the

32. Ballance, C.; Colledge, L., and Bailey, L.: Brit. J. Surg. 13:533 (Jan.) 1926.

33. Platt, Harry: Brit. J. Surg. 13:409 (Jan.) 1926.

peripheral nerves there were only two in which the ulnar nerve was found encased in callus. The nerve bed was often found to be altered, however, in such a way as to produce pressure or friction. Early involvement of the nerve is rare (nine out of 252 cases) and occurs most commonly in conjunction with fracture of the internal condyle. It is usually due to the primary contusion of the injury and tends to get well. Operation is indicated only after failure to improve at the end of a considerable period. When the symptoms develop after a latent period, the involvement is due to an alteration in the nerve bed, and operative treatment is usually necessary. Late involvement may occur as a remote sequel of fracture of the external condyle in childhood, and is due to friction or tension of the nerve. This condition necessitates operative treatment, either anterior transplantation of the nerve or correction of deformity by supracondylar osteotomy. Recurring dislocation of the nerve from its bed is due to a change in the configuration of the post-condylar groove, and transplantation of the nerve to the front of the elbow is indicated.

Periarterial Sympathectomy: An Easy and Rapid Method.—Camera³⁴ has devised a technic to obviate some of the difficulties of periarterial sympathectomy by the usual method. After isolating the artery and lifting it on a hook, he introduces a long slender needle into the vessel wall and passes this downward between the superficial and muscular coats for its entire length. He then slowly injects sodium citrate solution, withdrawing the needle as the injection is made. By this means the adventitia is distended and separated from the inner layers and can then be readily stripped away by scissors or scalpel dissection. He reports that Leriche has used this method since it was called to his attention and seemingly finds it helpful.

Effect of Periarterial Sympathectomy of the Renal Artery.—Melzner³⁵ has done periarterial sympathectomy on the renal artery in dogs, but was unable to perceive the slightest histologic change in the kidney after an interval of from three to seventy days. From his experiments he concludes that there is a segmental arrangement of the nerve supply of the vessels and that the operation of periarterial sympathectomy in general produces no marked effect on the circulation.

Operations on the Peripheral Nerves as a Substitute for Periarterial Sympathectomy.—As sympathectomy is not without risks and is attended by conflicting and irregular results there is a beginning tendency to turn to the peripheral nerves and to attempt to obtain vasodilatation by means of various procedures applied directly to them. Thus

34. Camera, Ugo: *Chir. d. org. di movimento* 10:195 (Dec.) 1925.

35. Melzner, E.: *Arch. f. klin. Chir.* 136:427, 1925.

and hyperthermia, which last for from seven to fourteen days. Ulcers and wounds are stimulated to heal, and pain from circulatory deficiency is relieved. That any permanent benefit results has not been established, nor have impartial observers noted any real improvement in cases of thrombo-angitis obliterans or in obstruction due to arteriosclerosis. In addition, the operation is not without risk, as shown by the report of several disasters. We are of the impression that less will be heard of this operation as time goes on, and we would hesitate to recommend it ourselves in any but exceptional conditions. As the effort to find a substitute for periarterial sympathectomy in operations on the nerves, this is to be encouraged, but the work should be done in the laboratory on animal subjects under proper control. We cannot too strongly condemn the trial of surgical innovations on human patients when their value can be determined by animal experimentation.]

FRACTURES

The Value of a Fracture Service in Hospital Organization.—Scudder³⁹ emphasizes the necessity of making individual surgeons responsible for the care of each fracture case from the accident ward, through the period of hospitalization down to and including the period of convalescence when the patient is under treatment in the outpatient department. In the later stages the social service worker is most important in bringing about a spirit of cooperation that is entirely lacking in most of our hospitals today. The work of the whole fracture organization has but a single object, that of getting the man back on his job. Standardized equipment and a trained personnel are needed. A special fracture service provides better opportunities for treatment and helps to raise the standards of treatment in general practice.

Fractures About the Elbow Joint.—Ritter, Basher, Wurtzel and Goldblatt⁴⁰ conclude from a study of 150 cases of fracture about the elbow with known end-results in fifty-two cases that the results obtained in the treatment of these injuries are often most unsatisfactory from the standpoint of both function and deformity, although failure of union almost never occurs. They have nothing new to suggest in the way of treatment, contenting themselves with the stereotyped formula that with the exception of fracture of the olecranon the patients should all be treated with the elbow fully flexed and the forearm supinated. They emphasize the need of proper reduction, which is to be accomplished by complete flexion of the elbow with downward traction on the

39. Scudder, C. L.: Bull. Am. Coll. Surgeons, Jan., 1926, p. 32.

40. Ritter, H. H.; Basher, W. W.; Wurtzel, G. L., and Goldblatt, Davis: Fractures About the Elbow Joint, J. A. M. A. 86:680 (March 6) 1926.

forearm. They feel that early functional restoration is dependent on early motion and massage.

[ED. NOTE.—We feel that improvement in results may be obtained in many of the elbow fractures by more frequent resort to the open method. Only by this means can complete reposition of fragments be secured in the comminuted intra-articular fractures and if they are fixed securely by internal splints movement and massage may be begun at once.]

End-Results in Fractures of the Femur.—Ashhurst and Crossan⁴¹ have made a study of 111 consecutive fractures of the femur. Of the ninety-eight patients who survived their injuries, eighty-seven, or 89 per cent, were traced. Among these eighty-seven patients, anatomic reposition of the fragments was secured in forty-four, or 50 per cent. Moderately accurate reduction was obtained in thirty-four, or 40 per cent, and in nine only was the position of the fragments bad at the time of consolidation. Fifty-five patients, or 63 per cent, had no functional disability whatever; twenty-six, or 30 per cent, had moderate functional disability, and only six, or 7 per cent, were incapacitated. Nearly 64 per cent of the patients returned to work in less than six months; nearly 84 per cent returned in less than nine months. For fractures through the neck and trochanters, either the abduction cast was used or the patient was treated as for fracture of the shaft of the femur, the choice depending on the level of the fracture and the best method of overcoming the deformity. For fractures of the shaft and most supracondylar and intercondylar fractures, Buck's extension was employed, with the patient's leg resting on a sliding splint to overcome friction. Operation was employed in 9 per cent of the cases, and less often in recent years than formerly—only three times in the last eight years.

Fractures of the Ankle.—Platt,⁴² writing on fractures of the ankle, follows Ashhurst's method of classifying them according to mechanism into fractures by external rotation, by abduction, and by adduction. He advises closed methods of treatment for fractures with a small amount of displacement. Out of 116 cases the open method was employed in only four. His study of end-results showed increasingly good functional results in 90 per cent after two years.

Ununited Fractures.—Henderson⁴³ has made a study of 259 cases of ununited fracture that were treated at the Mayo Clinic in the last

41. Ashhurst, A. P. C., and Crossan, E. T.: Prognosis and Treatment of Fractures About the Elbow Joint, J. A. M. A. 86:680 (March 6) 1926.

42. Platt, Harry: Fractures in the Neighborhood of the Ankle Joint, Lancet 1:33 (Jan. 2) 1926.

43. Henderson, M. S.: Ununited Fractures, J. A. M. A. 86:81 (Jan. 9) 1926.

six years. These were divided on an arbitrary basis into ninety-six cases of delayed union and 163 cases of nonunion. Included in the latter group were twenty-eight cases of ununited fracture of the hip, the results in which are considered separately. All of the 259 patients were treated surgically, the operative procedures being classified either as bone grafts or plastic operations. For grafting purposes usually the massive type of graft was employed. Plastic operation was the term applied to any procedure in which the fragments were shaped and fitted to each other and fixed by various means but without the use of a graft. A bone grafting operation was done in forty-three cases of delayed union and resulted in a cure in forty of the forty-two patients traced (96.2 per cent). Of the 163 cases of nonunion, the bone graft was used in 104, with cure in eighty-one of the ninety-eight cases traced (82.6 per cent). In the combined group the bone graft produced a cure in 86.4 per cent of the patients treated. In twenty-two cases of nonunion of the hip, bone grafts were used, usually from the fibula, and bony union resulted in sixteen of the twenty-one patients who were followed. Plastic operations in one form or another were performed in fifty-five cases, exclusive of the hip, thirty-two being classified as delayed union and twenty-three as nonunion. Cure resulted in 93 per cent of the cases of delayed union, but in only 65 per cent of those with nonunion. Five of the patients with nonunion of the hip were not considered suitable for bone grafting and they were subjected to the plastic operations of either Whitman or Brackett. Satisfactory results were obtained in all. The cases were carefully studied from the standpoint of etiology, and the outstanding factor appeared to be severe direct injury, so severe that there was no question as to its importance in the devitalization of the tissues. Sixty-two of these severe injuries were associated with compound fractures and fifty-six with simple fractures. Forty-seven compound fractures were encountered in the cases of nonunion, whereas only fifteen were in the delayed union group, showing that severe injuries with compound fracture are prone to lead to nonunion. A severe injury with a simple fracture appeared responsible in fifty-six of the cases. Inadequate fixation appeared to be responsible in twenty-three cases; poor reduction, with or without interposition of tissue, in forty cases; the presence of metal fixative material in eleven cases, and in thirty-nine cases no cause could be determined. Determination of the calcium and phosphorus content of the serum was made in practically all of the cases, but with indefinite results. The fact that a higher percentage of cures was obtained by both methods in the cases of delayed union, 93 per cent as compared with 73.8 per cent in the nonunions, leads him to conclude that the earlier an incipient nonunion is recognized and treated, the greater will be the chance of cure.

The Dangerous Period in the Development of the Hip Joint.—Harrenstein⁴⁶ believes that unfavorable mechanical conditions at the hip during the later months of pregnancy may bring about dislocation of the hip before the birth of the child. He has examined ninety-five pelves of fetuses, new-born babies and adults, and believes that the depth of the pelvis is least during the period when the length of the body is from 36 to 60 cm.; that the female pelvis is shallower than the male, explaining the greater frequency of dislocation in the female; that the left acetabulum is shallower than the right, explaining the greater frequency of left dislocation. LeDamany has found that in France the right acetabulum is deeper than the left; this differs from the reports from England, Germany and Austria. The female acetabulum is more sagittal and vertical than the male. He emphasizes the fact that during the 36 to 60 cm. period of fetal development the posture of the fetus is favorable to subluxation at the hip.

The Question of Reunion of Osteochondritic Joint Mice.—Lehmann,⁴⁷ in observing a series of early, not yet fully separated osteochondritic, potential joint mice, has found not only pseudarthritic processes, but also bridges between the subchondral tissue, and the osteochondritic area, suggesting that complete reconstruction is possible.

The Changes in Metabolism Associated with Fracture.—Dannheiser⁴⁸ has checked the work of Rehns on the muscle reaction to electricity in fracture of the bones. In the first week the muscles show decreased irritability, so-called stupor. In the following four weeks there is gradually increasing irritability, approaching the tetanic state. After four weeks the muscles gradually return to normal. The urine is acid for from six to twelve days, then alkaline for about a week, returning to normal thereafter. The hydrogen ion concentration in the urine was found to be similar to the findings of Rehns.

The Vertebral Column from the Anatomic and Physiologic Standpoints.—Gallois and Japiot⁴⁹ have observed that the vertebrae have an internal architecture following a perfectly definite rule. The bony lines follow practically the rules laid down by Julius Wolff in his description of the neck of the femur and the os calcis. The lines of bone are vertical, oblique and horizontal, and form two systems of support, a principal and an accessory. The principal lines of support are vertical. These lines exist in all the vertebral bodies and follow in line as if the intervertebral disks did not exist. They begin at the axis and extend to the sacrum. This gives a unity in the vertebral column and an indi-

46. Harrenstein, R. J.: *Ztschr. f. orthop. Chir.* 46:481, 1925.

47. Lehmann, J. C.: *Deutsche Ztschr. f. Chir.* 88:192, 1925.

48. Dannheiser, F.: *Arch. f. klin. Chir.* 136:292, 1925.

49. Gallois and Japiot: *Rev. de Chir.* 63:688, 1925.

viduality to each vertebra. The accessory system of support unites the body of the vertebrae by oblique and horizontal lines, two superior and two inferior. From the rectangular point of view, the vertebra is divided into two parts, a massive body and the apophysis. The bodies are supportive and the apophyses are the levers that control them by means of the muscles. The architecture of the different parts of the vertebrae corresponds to the laws established by Culman for the neck of the femur. The architecture of the vertebrae seems to be planned for two purposes: (1) to resist compression and (2) to permit the control of motion by the apophyses without lessening the supportive quality of the spine and without injury to the spinal cord and the nerves coming from it.

Experimental Research on the Regeneration of Articular Cartilage.—Haebler,⁵⁰ using dogs, has performed twenty-two experiments, the purpose of which was to determine the healing power of articular cartilage. When the cartilage alone was injured without injury to the subchondral bone, the wound in the cartilage showed no change after 300 days, showing that the cartilage itself has no power of regeneration. When the subchondral bone is injured as well as the cartilage, the cartilage defect is filled with fibrous tissue. The cartilage beyond the area of injury remains normal. He found that altered function of the joint, such as is produced by amputation, plaster-of-paris, or other lesion, results in arthritic changes in the cartilage.

MISCELLANEOUS

Lumbarization of the First Sacral Vertebra and Spondylolisthesis.—Léri⁵¹ gives such an excellent diagnostic symptomatology of the lumbarization of the first sacral vertebra and its forward slipping that it is worth reporting. He considers the clinical picture very characteristic. The onset of the trouble is often attributed to a definite trauma, such as a fall from a horse or a ladder. Even before the roentgenogram is studied the stance of the patient is suggestive. Some lateral deviation of the spine may often be observed and the sacrum is more prominent. The examining finger will feel a marked depression at the fifth lumbar vertebra. The shoulders are squared. The waist appears shortened and the abdomen more prominent. The lower part of the spinal column is farther forward than normal. When the patient bends backward the lumbar angle is increased, and when he leans forward this angle does not entirely disappear, and no normal lumbar kyphosis is produced. Most of the motion in the spine is dorsolumbar instead of lumbar. The walk often suggests a waddle. The pain, which has often

50. Haebler, C.: Beitr. z. klin. Chir. **134**, 1925.

51. Léri, André: Presse méd. **332**:1681 (Dec. 23) 1925.

existed for years, is usually nagging rather than intense and is felt in the region of the lumbosacral junction medially or laterally. As a rule, it does not radiate along the nerves and may resemble that of Pott's disease. It is not relieved by sitting, but only by lying flat with the knees flexed, a pillow under the back, and the head and neck supported. Any increase in the lumbar lordosis increases the pain, and high heels are uncomfortable. Going downstairs is harder than going up. If the patient jumps from a step he is often obliged to bend forward and to straighten up very gradually. The hip and lower leg motions are normal, as are also the reflexes and the skin sensations. The absolute diagnosis can be made only from the roentgenogram. The lumbarization of the first sacral vertebra may be much more pronounced on one side than on the other, or quite symmetrical on both sides, and the anomalies may be very complicated. In extreme cases the sixth lumbar or lumbarized first sacral vertebra appears almost suspended in the pelvis, and in these cases discomfort and pain may be very severe.

The Care and Cure of Crippled Children.—An editorial⁵² in the *British Medical Journal* and a little book by Girdlestone⁵³ show how determined an effort is being made in Great Britain, especially in England, to ameliorate the condition of the cripple and provide for his complete rehabilitation. The British Central Committee for the Care of Cripples now supports 5,000 beds for this purpose. Twenty per cent of the forty counties have orthopedic clinics. The general plan includes a central hospital for the more acute and operative cases, accessory town clinics, and country fresh air hospitals for patients requiring heliotherapy, education and industrial training. Moreover, propaganda for the education of the medical and lay public has been started in order to combat the underlying causes of the diseases that produce crippling by inducing a general adoption of more hygienic methods of living.

52. Editorial, *Brit. M. J.*, Dec. 12, 1925, p. 1133.

53. Girdlestone: Bristol, John Wright and Sons, 1925.

(Concluded)

CORRECTION

MECHANISM OF BACTERIAL INFECTION

In Dr. Wilensky's article on this subject, in the August issue of the *ARCHIVES OF SURGERY*, the legend for figure 3 was incorrect. It should have read: Fig. 3.—Comparison should be made with case 7 in the text.

Correspondence

"THE RELATION OF THE BONE MARROW TO THE LYMPHATIC SYSTEM"

In his article on the subject in the November, 1925, issue of the ARCHIVES OF SURGERY, Kolodny has suggested that the bone marrow is supplied with lymphatic channels, although this has been denied by a large number of writers, of whom I am an unrepentant one. He adduces a certain amount of evidence for his contention, and it seems to be necessary to point out that other interpretations of it are possible, and are, to my mind, more probable.

His evidence is obtained from the results of injection of India ink into the medullary cavity and subsequent recovery of it from "regional" lymphatic glands: this is admittedly a summary review of his admirable experiments, but it does, I think, bring out the essential principle. There is one question that immediately arises: Is there any good evidence that the India ink, which lodges in the local lymphatic glands, reaches them by way of lymphatic channels? It must be recollected that, if India ink is injected intravenously, some will be found in the lymphatic glands, and here there is no special reason for supposing that it has all arrived at this site after traveling along lymphatic channels. If, therefore, India ink can reach lymphatic glands from the blood stream, it is surely possible that this is the mechanism by which it did so in Dr. Kolodny's experiments. This is an even greater probability when it is recollected that the India ink was injected directly into the medullary cavity and not into any definitely known and recognizable channel.

The evidence obtained in this manner by Kolodny is amplified by reference to the process of metastasis of malignant epithelial tumors. He states that in metastatic carcinoma of the bone veins filled with carcinomatous cells are easily found, but he does not mention that these may be found even inside the bone marrow, whereas intramedullary lymphatic channels filled with such cells have never been described. (Piney, A.: *Brit. J. Surg.* 10:235 [Oct.] 1922; 11:707 [April] 1924.)

I think that I am not misinterpreting Kolodny when I presume that he regards the deposition of carcinomatous cells in the bone marrow as being the result of permeation of the lymphatic channels. If this were really the case, it would not be possible to understand how such metastases could occur in association with extremely small early carcinomas, as is not infrequently the case. The description of invasion of bones by retrograde lymph flow from hypogastric lymph glands in cases of carcinoma of the prostate is not really convincing; many cases of bony metastasis in the femora (derived from a primary growth in the prostate) are on record, but the hypogastric lymph nodes are by no means invariably involved.

As in the preparation of juggled hare, it is essential first to catch the hare, in the present case it is necessary to find the lymphatic channel full of cancer

cells. Kolodny writes of Sampson Handley's lymphatic channels passing from muscle insertions to bones as being hypothetical, but the channels of which he himself writes are equally so; neither he nor Sampson Handley have seen the channels. The hematogenous origin of metastatic tumors of the bone seems to be sufficient explanation of the known facts, and did not William of Occam contend that "*entia non sunt multiplicanda praeter necessitatem*"?

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THE FORMATION AND TREATMENT OF FIBRO-ADENOMAS OF THE BREAST

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In an article¹ I wrote in 1923, I described for the first time a fibro-adenoma of the breast that began in the intra-elastica tissue of that gland. I feel sure it is a more common tumor than is generally supposed. I also described the formation of fibro-adenomas in general. The article to which I refer contains matter relating to other states of the breast and my description of fibro-adenomas in particular was rather buried among the other material. I am glad to have this opportunity of calling particular attention to the formation of fibro-adenomas only. I do not consider that any types of fibro-adenomas arise from so-called "rests," and it will be seen that I believe that they originate in parts of the gland that have been normal.

Figure 1 shows the two tissues from which the varieties of fibro-adenomas originate. The first tissue (fig. 1 *G*) I shall describe is that which exists immediately inside the elastica (fig. 1 *H*); the second tissue is the pericanalicular and periacinous connective tissue that immediately surrounds the ducts and acini (fig. 1 *K* and *K*₁) and which, with the ducts and acini it surrounds, is embedded in the general supporting fibrous tissue of the breast (fig. 1 *L*). For want of better descriptive terms, I shall describe those changes which occur in the connective tissue immediately internal to the elastica under a heading of "intra-elastica," and those changes which occur in the pericanalicular and periacinous connective tissue of "extra-elastica," although the pericanalicular tissue is not immediately external to the elastica but is separated from it by the structures composing the duct wall. Hence it is important to describe the distribution of the elastica of a normal breast. This tissue surrounds all ducts and terminates abruptly when the acinus

1. Cheatle, G. L.: Hyperplasia of Epithelial and Connective Tissues in the Breast: Its Relation to Fibro-Adenoma and Other Pathological Conditions, *Brit. J. Surg.* 10:436 (April) 1923.

is reached. It is not uncommon in some breasts for the elastica to surround or partly surround at least some acini in a lobule. When this occurs the elastica of the acini and ducts is continuous. Occasionally the elastica surrounds a lobule. The intra-elastica tissue normally consists of bipolar cells which are sparsely scattered in very delicate fibrillous tissue. Separating this tissue, which is immediately internal to the elastica, from the epithelium lining the ducts and acini, is a single continuous layer of nonstriated muscle fiber (fig. 1 *E*). This intra-elastica tissue is present in all ducts and acini. It surrounds the latter even when the elastica is not continued around them (figs. 1, 2, 3 and 4). It is from these two component parts of the intra-elastica connective tissue that the intra-elastica fibro-adenomas arise; hence, it is not uncommon to notice strands of nonstriated muscle fibers scattered about in the connective tissue of the fibro-adenomas belonging to this class.

I. INTRA-ELASTICA FIBRO-ADENOMA

Hyperplasias of the intra-elastica tissue occur in older women than those of the extra-elastica type and usually all forms of it affect women who are in the late thirties and onward. Both types usually affect the terminal parts of the ducts and acini. Hyperplasia of this tissue I divide into two parts: (*a*) diffuse and (*b*) local.

(*a*) *Diffuse*.—In this type there is a general, more or less uniform, hyperplasia of the tissue (figs. 2 and 3) which early undergoes degeneration (fig. 4), and instead of being composed of recognizable cellular tissue it appears as a uniform state in which no cells can be detected; it stains diffusely. It affects discrete portions of the gland and I have never seen it generalized throughout the whole gland. It appears clinically when it affects ducts and acini as a localized lumpiness and is always diagnosed in that meaningless term "chronic mastitis." Needless to say, it has nothing to do with inflammation. It may affect terminal parts of ducts alone, acini alone, or terminal parts of ducts and acini (figs. 2 and 4).

(*b*) *Localized*.—The hyperplasia in this state is represented by a well marked tumor and forms one kind of intracanalicular fibro-adenoma. The tumor may be represented by a purely acinous fibro-adenoma (fig. 5), or by a pure intracanalicular duct fibro-adenoma (figs. 6 and 7). Both states respectively represent a single tumor. The acinous intra-elastica fibro-adenoma (fig. 5) never attains a large size and usually is discovered accidentally in examinations of the breasts for other lesions. The intra-elastica duct fibro-adenoma (fig. 7), on the other hand, appears as a definite tumor and therefore becomes of greater clinical

importance. The duct intracanalicular fibro-adenoma of this type arises from the diffuse affection of the duct and appears as a definite lobulated tumor, the connective tissue of which is composed of delicate fibrous tissue in which bipolar and ordinary cells are separated from each other by more or less delicate connective tissue fibers, among which can be seen separate and irregularly distributed strands of nonstriated muscle fibers. An early stage of this tumor formation is seen in figure 6. The epithelium covering the connective tissue is of healthy appearance, not so columnar in type as in normal breasts, and from this lining of epithelium, processes dip down into the connective tissue and form definite, vigorous, normal looking acini (fig. 8). Also, papillomatous processes from which secondary papillomatous processes grow may arise from the surface of the tumor and give rise to very complicated appearances (fig. 9). The patient from whom the sections were taken was 51 years of age and it is extraordinary to note how young and vigorous are the new epithelial formations in the tumor.

II. EXTRA-ELASTICA FIBRO-ADENOMA

The connective tissue in which the following changes begin is the pericanalicular and periacinous connective tissue that immediately surrounds ducts and acini (fig. 1 *K* and *K₁*). It separates these structures from the more dense and coarse supporting connective tissue of the breast (fig. 1 *L*) and, pathologically, is a more important tissue than the latter. There is no increase in ducts or acini in this type of disease. The changes occur in preexisting ducts and acini and hence it differs materially from the intra-elastica localized fibro-adenoma which occurs in the ducts and which I have described above. The changes I am about to describe occur in females of all ages from adolescence onward. Like the intra-elastica fibro-adenomas, the changes occur in the terminal parts of the ducts and acini, and also as (*a*) diffuse and (*b*) localized changes.

(*a*) *Diffuse Hyperplasia of the Extra-Elastica Fibrous Tissue (Diffuse Fibro-Adenomatosis).*—This may affect nearly the whole breast, giving rise to the appearance of a generalized fibro-adenomatosis. In this diffuse state parts can be seen in which the changes are more isolated than elsewhere (fig. 10). This isolated part exactly resembles those changes which I described under (*b*) the localized form. The epithelial change occurring in this state is mainly one of desquamative hyperplasia within the lumina and are characterized by their small, desiccated appearance and by their unwillingness to take up the stains. The diffuse form generally occurs after the age of about 30 years, and some observers do not consider that this diffuse fibro-adenomatosis is of

precisely the same character as that which is occurring in the localized form. I can only say there is no difference between the localized and diffuse forms in their growth and microscopic appearance. I regard both states as being primary and not merely the result of chronic inflammation.

(b) *Localized Hyperplasia of the Extra-Elastica (Fibro-Adenoma)*.—The terminal ducts and acini are, as a rule, the only parts involved in this tumor. The epithelial changes are the same desquamative type that occur in the diffuse form. The coarse fibrous tissue which supports the breast is pressed on by the growing tumor and here there are appearances that give rise to the false conception of a capsule. I have never been able to detect a real capsule to any of these tumors. It is important to observe that the tumor increases in size by two methods. The first is a continued growth of periacinous and pericanalicular connective tissue that was first affected (fig. 11 *A*), and the second an increase of the pericanalicular and periacinous fibrous tissue of fresh ducts and acini (fig. 11 *B* and *C*). The latter may be in juxtaposition to the original tumor, or they may be separated from it by parts of the breast that appear to be nearly normal. Lobulation of the tumor is accounted for in this way. The importance of this observation determines the inevitable conclusion that even a localized fibro-adenoma is really a process affecting consecutively parts in a localized area of a gland that had been normal. The ducts and acini in these tumors may become cystic. Into the cysts may grow intracanalicular and intra-acinous projections. In some of these projections I have noticed that the intra-elastica connective tissue has become diffusely hypertrophied.

CLINICAL SIGNS

The clinical signs of the diffuse forms of the intra-elastica and extra-elastic changes I have described are those of lumpiness of the breasts in thin people. In fat people they give rise to no definite clinical sign. The lumpiness is due to fat lobules and the underlying breast cannot be palpated. Lumpiness of a breast includes hosts of more important changes, generally summed up in that meaningless diagnosis of "chronic mastitis." The clinical sign, nodularity of a breast, includes early and late carcinomas as possibilities.

The clinical signs of the localized intra-elastica and extra-elastica hyperplasias give rise to a lobulated, defined, solid tumor commonly known as a fibro-adenoma. The tumor may be single in the breast, or it may appear to be single, and microscopic examination reveals unsuspected tumors in its neighborhood, or the tumors may be obvious

clinically as being multiple. The diagnosis from a duct carcinoma in which the tumor is not adherent to the skin is as follows: A duct carcinoma is rounded and not lobulated. There may be a history of a discharge of blood or serum, or both, from the nipple. In its later stages the tumor becomes attached to the skin and there may or may not be enlarged glands in the axilla.

TREATMENT

It will have struck the reader that when all forms of intra-elastica and extra-elastica hyperplasia are localized and form a definite tumor, a segment of the breast is involved, and hence the only rational treatment that can be adopted is to excise the whole of the affected segment that includes the tumor. This statement applies to all forms of fibro-adenomas and it is not safe to attempt only a so-called enucleation of the tumor. I have established the fact that in the formation of fibro-adenomas a segment of the breast is undergoing the change, and thus a cure by an enucleation of the tumor is effected by a pure accident (fig. 11).

The diffuse forms usually require no treatment. When doubt enters the mind of the surgeon, then I believe the safest course is to remove a large part of the gland for the purposes of a diagnosis, which can be made only by making whole sections of the part removed. The importance of a definite diagnosis in glands of this type becomes clear when it is realized that carcinoma may diffusely affect a whole breast and the condition clinically resemble the diffuse fibro-adenomatous states. In my experience such patients have always been lulled into a false sense of security by being sent away with the utterly meaningless diagnosis of "chronic mastitis," a term that I feel sure should be abolished from the nomenclature.

My observations have been based on the results of microscopic examination of whole sections of the breast in which the elastica has been stained.

SUMMARY

1. The changes described in this article occur in the terminal parts of ducts and acini and in tissues that have been normal.
2. Diffuse hyperplasia and the formation of intracanalicular fibro-adenomas occur in the intra-elastica tissue.
3. Diffuse adenomatosis and fibro-adenomas arise from the pericanalicular and periacinous (extra-elastica) connective tissue. The fibro-adenomas of this type may contain intracanalicular growth which may show diffuse hyperplasia of the intra-elastica connective tissue.

4. The formation of intra-elastica and extra-elastica fibro-adenomas is a progressive process that affects consecutively fresh parts of a segment of the breast that has been normal and accounts for the lobulation of the tumor.

5. The correct treatment of fibro-adenoma is to excise the affected segment of the breast that contains the tumor or tumors.

6. I wish it to be particularly noted that nodularity or lumpiness of a breast can be detected only in thin subjects. In fat people nodularity of the breast is often described, but the nodularity is due to lobules of fat only.

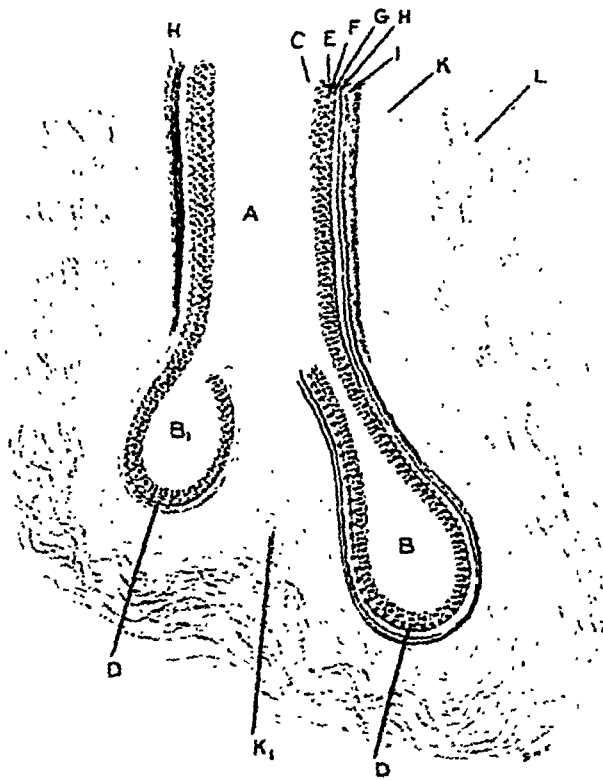


Fig. 1.—Terminal duct and two acini (diagrammatic): *A*, interior of duct; *B* and *B*₁, interiors of two acini; *C*, lining of epithelial cells. The abrupt change of character that takes place in the epithelium, *D*, of the acini is not shown; *E*, unstriated muscle fiber; *G*, intra-elastica connective tissue; *H*, the elastica; *I*, the muscular tissue of the duct; *K*, the pericanalicular connective tissue; *K*₁, the intra-acinous connective tissue; *L*, the supporting connective tissue of the breast in which all the foregoing are embedded.



Fig. 2.—The terminal duct and acini in which is seen diffuse hyperplasia of the intra-elastica connective tissue: *A*, interior of the ducts; *B*, an acinus that has the elastica continued around it; *C*, the elastica; *D*, intra-elastica connective tissue; *E*, the epithelial lining; *F*, acini showing hyperplasia of the intra-elastica shown in this group of acini. The intra-acinous connective tissue is well

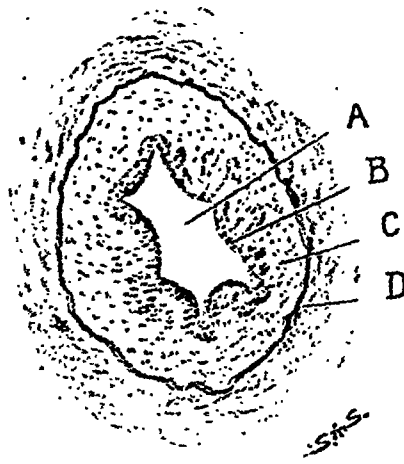


Fig. 3.—Terminal branch of a duct: *A*, the interior of the duct; *B*, its epithelial lining; *C*, the hyperplasia of the intra-elastica connective tissue; *D*, the elastica which itself has undergone a little hyperplasia.

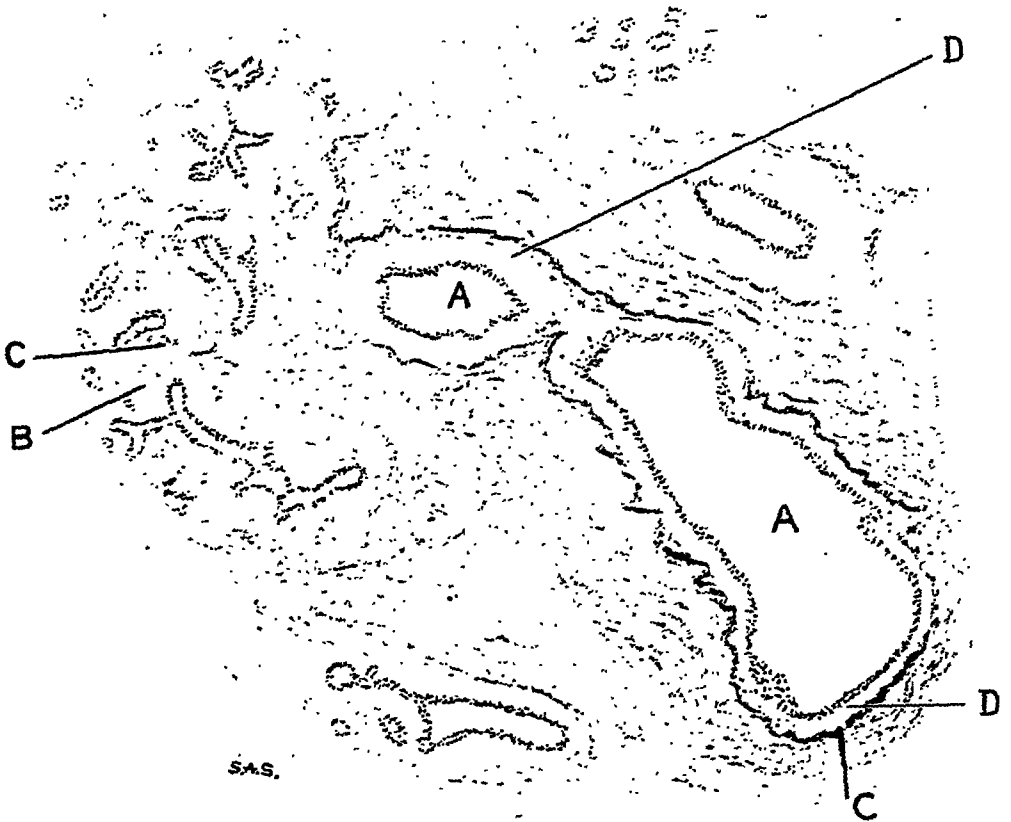


Fig. 4.—Terminal duct and acini: *A*, the interior of the duct; *B*, the intra-elastica connective tissue of the acini which can be traced in direct continuity with the intra-elastica tissue of the duct; *D*, the intra-elastica tissue around these structures has undergone some degeneration; *C*, the elastica which has undergone some hyperplasia.

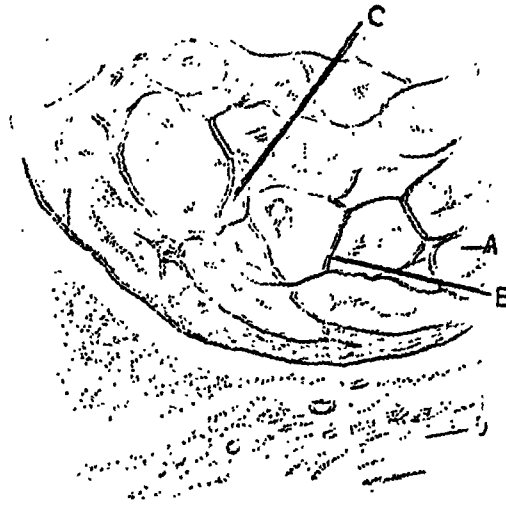


Fig. 5.—Hyperplasia of the intra-elastica tissue surrounding acini which has formed a definite intra-elastica acinous fibro-adenoma; this was discovered accidentally in examining a breast for carcinoma: *A*, the intra-elastica connective tissue which has undergone complete degeneration; *B*, the elastica which surrounds all the acini of this lobule; *C*, the intra-acinous connective tissue, and *D*, surrounding tissue.

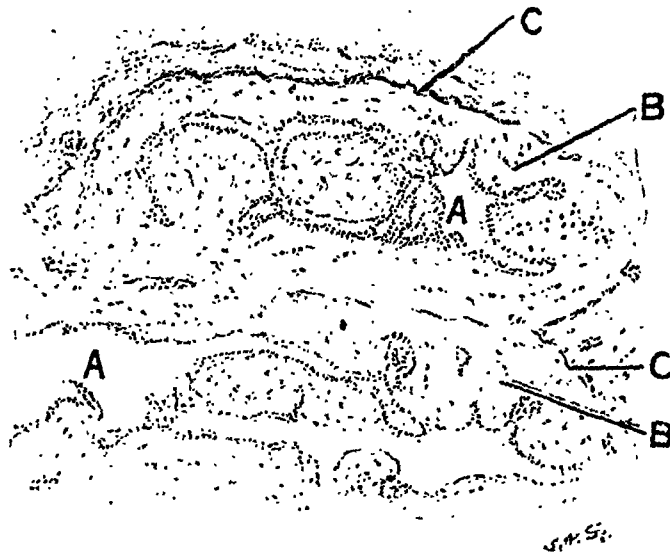


Fig. 6.—Two parts of a convoluted terminal duct which show the beginning of a definite intracanalicular intra-elastica fibro-adenoma: *A*, interior of the duct; *B*, the intra-elastica connective tissue which is forming papillomas lined by epithelium which are growing into the interior of the duct; *C*, the elastica.

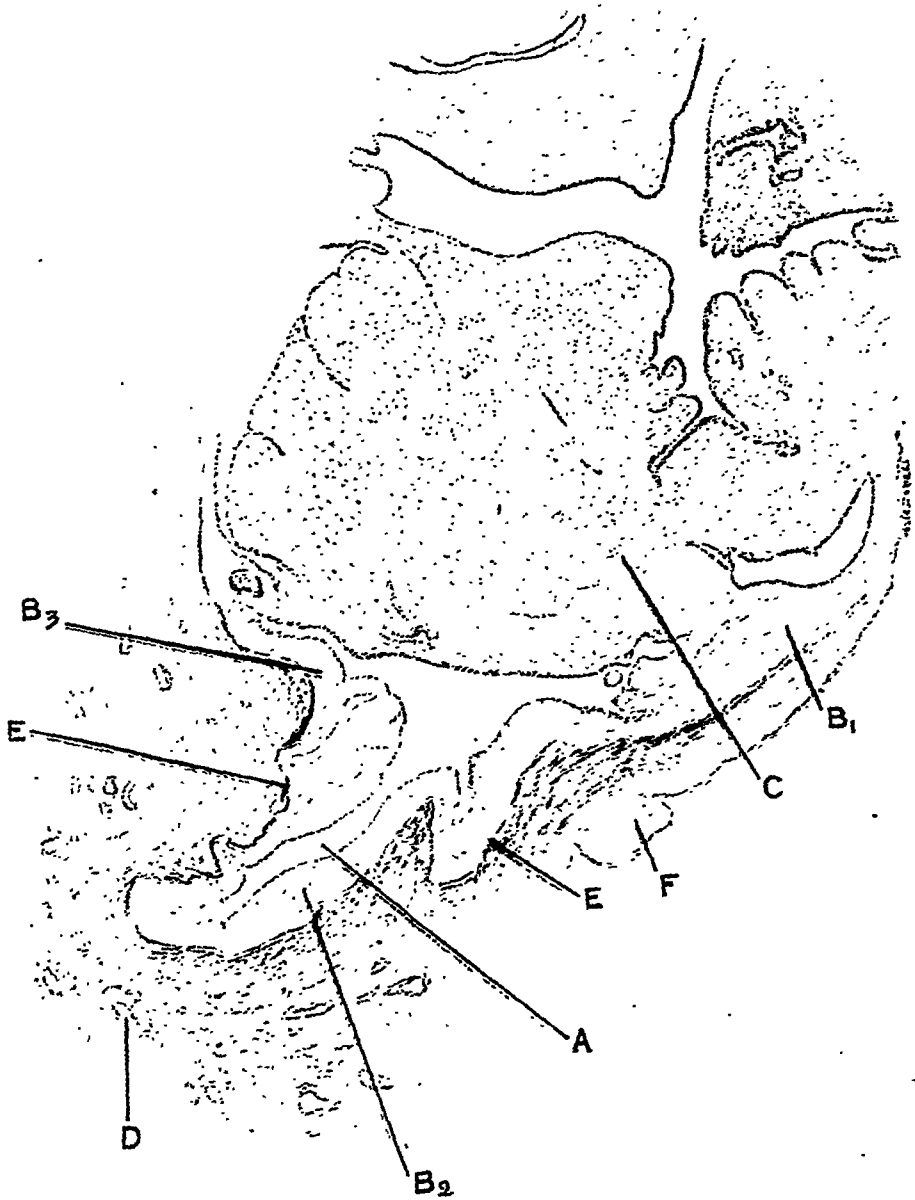


Fig. 7.—Part of an intra-elastica intracanalicular fibro-adenoma, the whole of which was the size of a walnut, from the breast of a married woman, aged 51: *A*, the interior of the terminal duct; *B*₁, *B*₂ and *B*₃, the intra-elastica connective tissue of this terminal duct which has undergone diffuse hyperplasia and from which the fibro-adenoma can be seen growing at *C*; *E*, the elastica; *F*, part of the same tumor in the same duct that was convoluted; *D*, an acinus that has undergone diffuse intra-elastica hyperplasia which has degenerated.

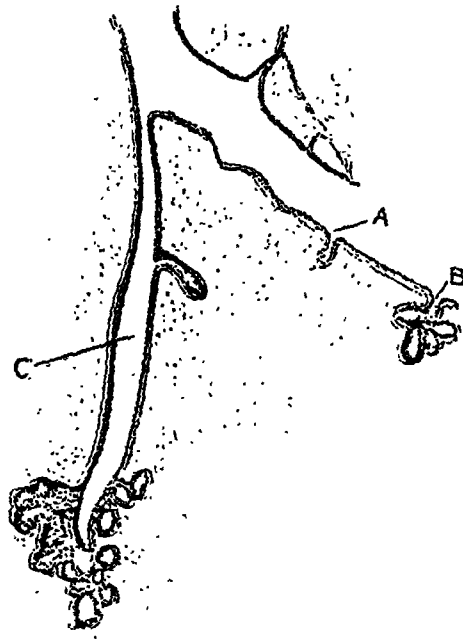


Fig. 8.—A duct and its acini which has dipped down into the tumor *C* of figure 7 from the epithelial surface lining it; *C*, duct and acini; *A*, a simple epithelial prolongation; *B*, acini without any duct formation.

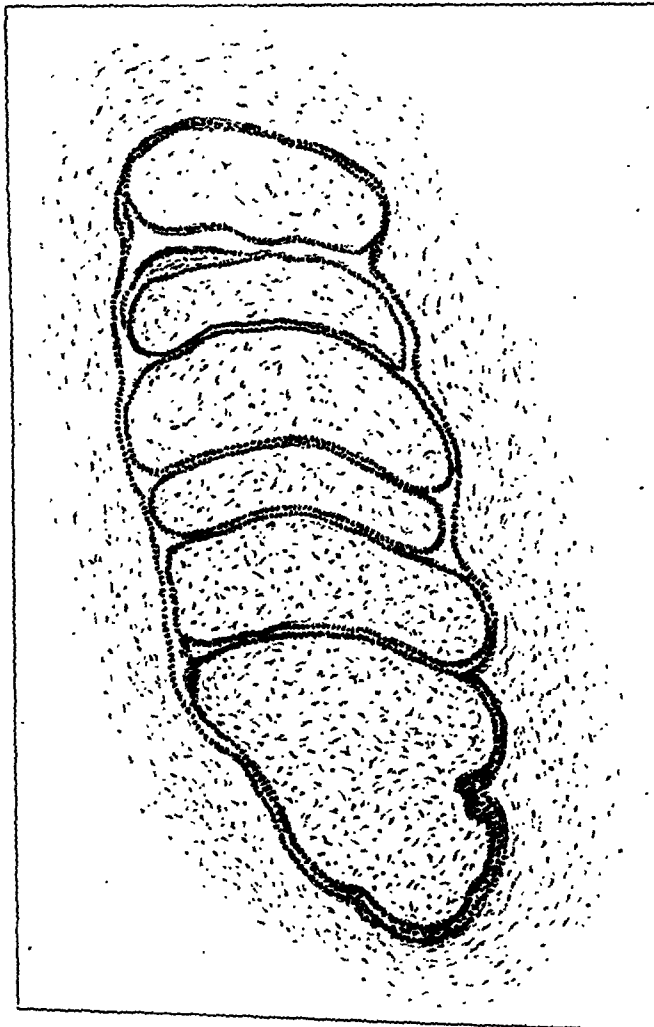


Fig. 9.—The complicated appearance to which the formation of papillomas and secondary papillomas gives rise in this class of tumor.

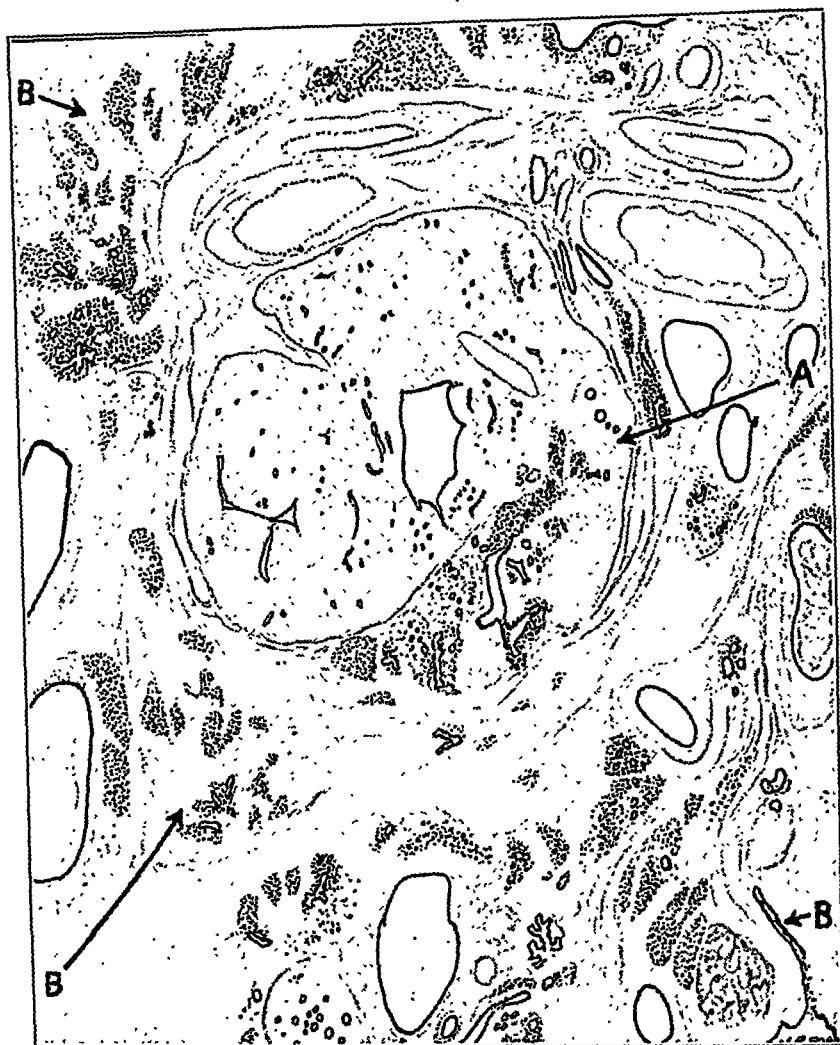


Fig. 10.—Diffuse fibro-adenomatosis of the breast: The pericanalicular and intra-acinous connective tissue is seen to have undergone hyperplasia at *B, B, B*; at *A*, the process has resulted in the formation of a microscopic extra-elastic fibro-adenoma.

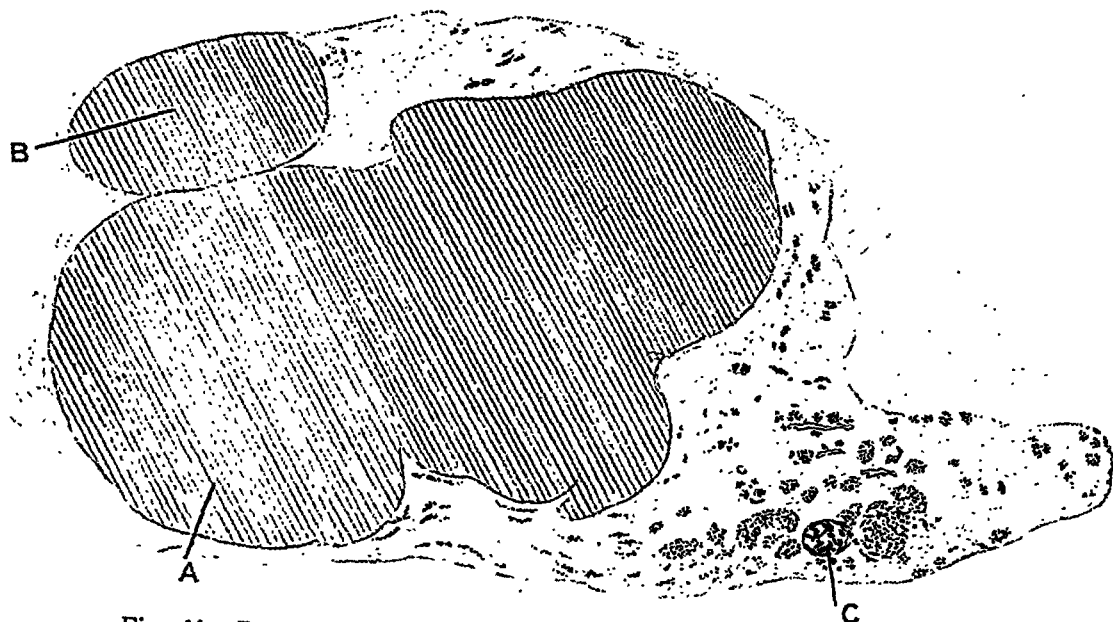


Fig. 11.—Process of formation of an extra-elastic fibro-adenoma in an unmarried woman, aged 27: *A*, main tumor of which *B* is a part; *C*, a small extra-elastic fibro-adenoma which is undergoing the process of formation.

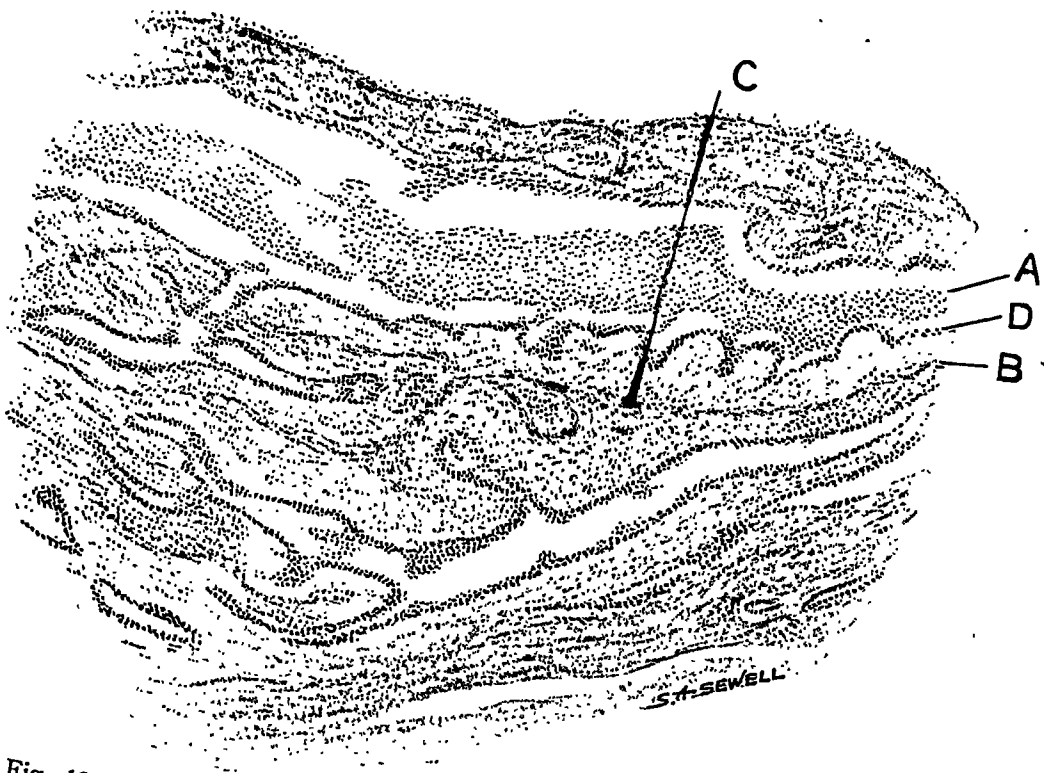


Fig. 12.—Intracanalicular formation within an extra-elastica fibro-adenoma; C, its elastica; B, the intra-elastica tissue which has undergone hyperplasia; D, its lining epithelium, and A, the desquamative epithelial hyperplasia that fills the cyst into which the intracanalicular tumor grew.

THE EFFECT OF THE LIGATION OF THE PULMONARY ARTERY OF ONE LUNG WITHOUT AND WITH RESECTION OF THE PHRENIC NERVE*

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This article will detail late results following ligation of the left pulmonary artery in dogs, without and with simultaneous section of the phrenic nerve.

In a previous report¹ it was shown that the operative procedure is unassociated with any definite shock, that the animals regain normal activity within twenty-four hours and remain so until the experiment is terminated, as much as four months later.

In the interval included in the reported experiments, the lung with intact pulmonary artery expands and herniations in the thinnest areas of the mediastinum occur, but this process becomes stabilized after a month. On the other hand, the lung with ligated pulmonary artery gradually decreases in size, and this process progresses more rapidly when the phrenic nerve has been sectioned. Collateral circulation is established by increase in the caliber of the bronchial artery which doubles its size in three months but somewhat less rapidly when the phrenic nerve has been sectioned.

Microscopically, the alveolar walls become distended shortly after the operative procedure and hemorrhages occur in the alveoli followed by desquamation of the alveolar lining cells and phagocytosis. This in turn is followed by a new connective tissue formation which is more rapid when the phrenic nerve is cut than when the vessel alone is ligated.

The present series of experiments was undertaken to determine the extent of the fibrosis after longer time intervals.

METHODS OF EXPERIMENTATION

The experimental procedure was detailed in the previous report. Seven animals are included in the present series and in three of these the phrenic nerve was cut. The final observation was made two years after the beginning of the experiment. At necropsy the precaution of tying the trachea before opening the chest cavity was constantly observed.

* From the Brady Laboratory of Pathology and Bacteriology, Yale University School of Medicine, New Haven, Conn.

1. Schlaepfer, Karl: Ligation of the Pulmonary Artery of One Lung With and Without Resection of the Phrenic Nerve, Arch. Surg. 9:25-94 (July) 1924.

EXPERIMENTAL RESULTS

The results of these experiments are so similar to those included in the former report that the immediate purpose of this article will best be served by a brief summary of the changes in the whole series with special emphasis on the findings in animals at the end of two years after operation.

No deformity of the chest wall or of the spine was evident even after two years' observation. Roentgenograms taken at regular intervals showed the diaphragm at its normal level on both sides when the phrenic nerve was intact, but when it was resected, an elevation of the paralyzed diaphragm was conspicuous and became more and more marked as time passed (fig. 1).

The displacement of the mediastinum and heart was not satisfactorily demonstrated in roentgenograms because it proved impossible to obtain



Fig. 1.—*A*, chest three weeks, *B*, ten months, and *C*, two years after ligation of left pulmonary artery and resection of left phrenic nerve, showing gradual elevation of diaphragm on paralyzed side.

comparable pictures. The data obtained, therefore, are derived solely from necropsies. The lung with the intact pulmonary artery becomes distended and indents the mediastinum in its thinnest portions toward the lung whose pulmonary artery has been ligated. This results in the formation of hernias of the mediastinum, from 3 to 4 cm. deep. By the same process, the right mediastinal lobe becomes interposed between the left lung and the diaphragm. The process becomes stabilized after one month. The enlargement of the lung with intact pulmonary artery is partly due to compensatory emphysema. It is presumed that expansion results in part from a dilatation of the blood vessels in the alveolar walls.² There is not enough evidence at hand to indicate whether these

2. Von Basch: *Klinische und experimentelle Studien aus dem Laboratorium Prof. von Basch, Berlin* 1:171, 1891.

two factors are effective separately or whether they have any inter-relationship.

Excess fluid is not present in the pleural cavity and the pleural covering is thin and glistening everywhere except over the areas of fibrous adhesions, restricted to two well defined areas of trauma at



Fig. 2.—Posterior view of chest organs in dog 140 days after ligation of left pulmonary artery and crushing of left phrenic nerve; the left bronchial artery, *L. Br.*, is more than twice the size of the right one, *R. Br.*, although an intercostal vessel, *I. c.*, branches from the right bronchial artery.

operation: the site of ligation of the pulmonary artery along the mediastinum and the scar of operation in the anterior chest wall. Variations in the extent of adhesion formation are considerable: in a specimen of

one and one-half years' duration, for instance, only a few adhesions were present in the region of the hilum whereas in a specimen of two years' duration, the adhesions to the anterior chest wall and to the mediastinum were quite extensive.

The collateral, nutritive circulation through the bronchial artery is well established within two months after ligation of the pulmonary artery and within three months if the retarding action of the paralyzed

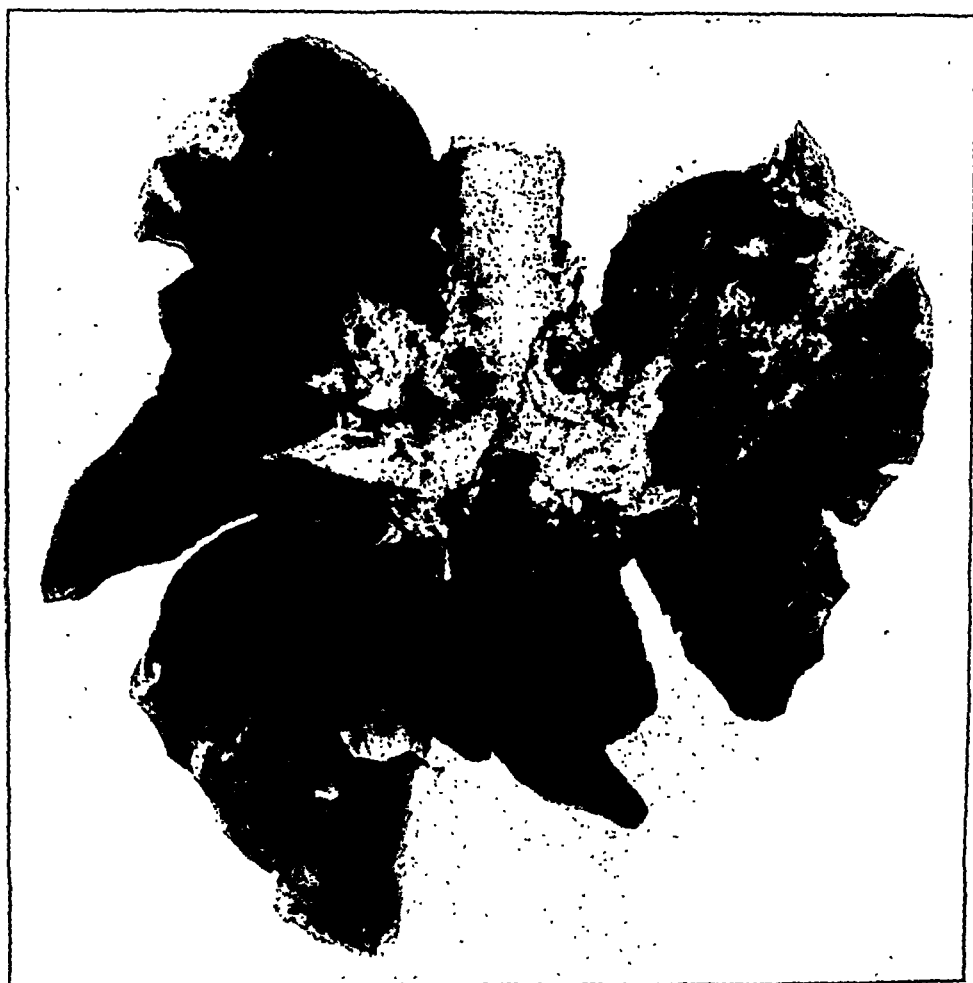


Fig. 3.—Lungs two years after ligation of left pulmonary artery and resection of left phrenic nerve.

diaphragm is present (fig. 2). The bronchial artery doubles its caliber within this time interval, and in the group without section of the phrenic nerve, is from three to four times the normal size at the end of two years. With a paralyzed diaphragm, the caliber of the bronchial artery generally does not exceed twice the normal even after two years.

Evidence of increased intrapulmonary pressure is forthcoming from the fact that hypertrophy of the right ventricle is encountered in experiments of one and one-half and two years' duration.

The lung with ligated pulmonary artery becomes reduced in size from four-fifths to three-fourths the normal after three months, and thereafter more slowly, reaching two-thirds the normal after two years.

Section of the phrenic nerve hastens this process. Within three weeks it is reduced to three-fourths; in three months to two-thirds; in five months to one-half, and varies after two years between two-thirds and half the original size (fig. 3).

From the beginning the lung with ligated pulmonary artery is firmer than the intact organ and remains so throughout the whole series. The increase in consistency is more marked in the lower lobe and especially if the phrenic nerve has been resected. It progresses slowly in the

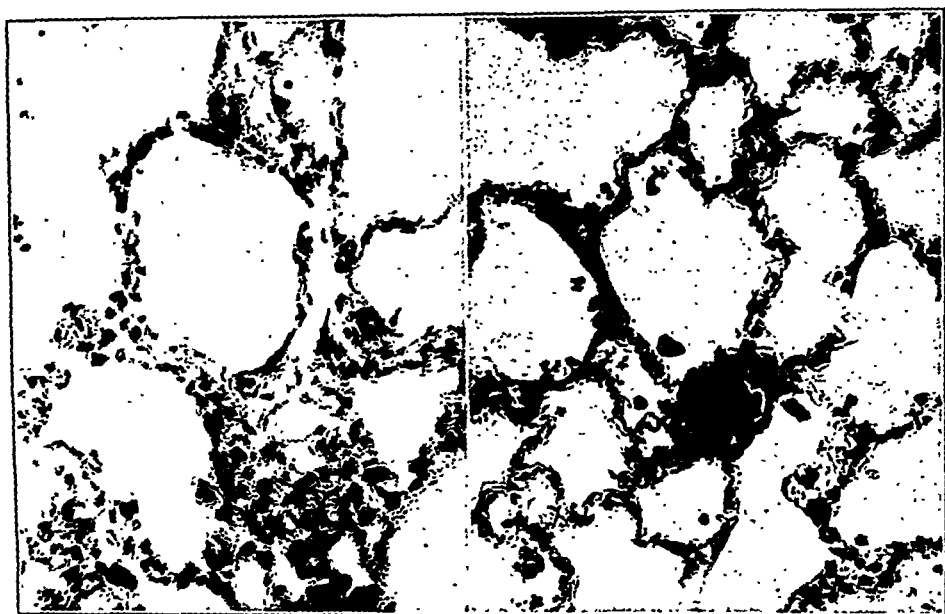


Fig. 4.—*A*, lung whose pulmonary artery was tied two years before; slight increase of connective tissue in alveolar walls and around medium sized blood vessels; *B*, opposite lung, which has a normal appearance; $\times 375$.

course of two years. After two years the difference of the lungs without and with section of the phrenic nerve is striking and justifies a separate description.

The difference between the right and the left lungs when only the pulmonary artery is ligated in the left is not striking. There is a slight increase in consistency of the upper and the lower lobes of the lung with ligated pulmonary artery associated with irregularly distributed, slight fibrosis of the bronchial and the alveolar walls (fig. 4, *A* and *B*).

When ligation of the pulmonary artery is combined with section of the phrenic nerve, the lung becomes mottled by the presence of small, whitish specks visible both on the pleural surface and on section. This change is most conspicuous in the lower lobe and diminishes toward the

apex. Injection of gelatin through the bronchial artery shows that branches of this vessel form the center of these white dots. These in turn are surrounded by air containing zones. Strands of connective tissue are especially numerous in sections through the lower lobe near the paralyzed diaphragm. They cross the field in different directions and separate groups of alveoli with irregularly thickened or almost normal alveolar walls. The walls of the bronchi, too, are thickened (fig. 5 *A*). The intact lung shows dilated, empty alveoli and congested blood vessels irrespective of the length of time of the experiment or the operative procedure (fig. 5 *B*).

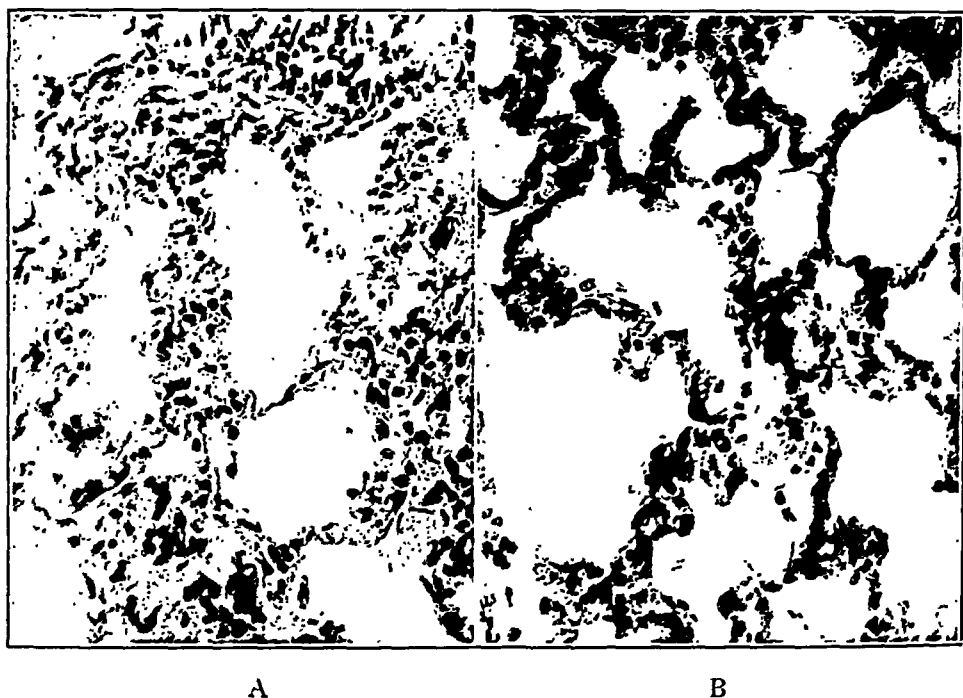


Fig. 5.—*A*, the lung whose pulmonary artery was tied and the phrenic nerve cut two years before; marked increase in connective tissue, especially around the larger blood vessels; *B*, opposite, intact lung, which does not show any connective tissue increase; empty alveoli and congested blood vessels are only findings of note; $\times 375$.

COMMENT

Two facts are evident:

1. The collateral circulation is more rapidly and more efficaciously established when the diaphragm is intact.
2. Fibrosis is more extensive when the diaphragm is paralyzed.

The explanation of these facts and their relative importance may be advantageously discussed. The deduction seems permissible that when the pulmonary artery is ligated and the phrenic nerve resected, there is increased stasis which considerably augments fibrosis of the lung. Perhaps the association with elimination of the piston-like action of the

diaphragm which facilitates the blood flow in the lung hampers the formation of an efficacious circulation through the bronchial artery and the pulmonary capillaries.

SUMMARY

1. Ligation of the pulmonary artery is associated with a fairly rapid development of a collateral circulation through the bronchial vessels, but even after two years the extent of the pulmonary fibrosis in the lung whose pulmonary artery is ligated is slight.

2. When ligation of the pulmonary artery is associated with simultaneous resection of the phrenic nerve, fibrosis of the lung is much more extensive, but there is a distinct retardation in the formation of a collateral circulation through the bronchial artery.

These two facts seem to be linked together as the most extensive fibrous reaction occurs about the radicals of the bronchial artery.

3. It is obvious that simple ligation of the pulmonary artery is not an efficacious therapeutic procedure to stimulate fibrosis of the lung in tuberculosis and that more beneficial results might be expected, in case the foregoing experiments are of any value, if ligation of the pulmonary artery is associated with simultaneous resection of the phrenic nerve.

4. A final factor worthy of mention is the evidence of increased intrapulmonary pressure after ligation of the pulmonary artery as expressed by the findings, both gross and microscopic, of right sided cardiac hypertrophy.

THE SKIN TRIANGLE OF APPENDICITIS

A DISCUSSION OF ITS SIGNIFICANCE AND ITS DIAGNOSTIC VALUE
AS OBSERVED IN MORE THAN FOUR HUNDRED CASES
OF ACUTE APPENDICITIS *

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NEW YORK

OBJECT OF ARTICLE

The object of this article is to report the value of skin tenderness in the diagnosis of acute appendicitis. The study was conducted in the Third Surgical Division of Bellevue Hospital, service of Dr. George David Stewart, and is based on 428 consecutive cases, over a period of six and one-half years. In a previous article from this division¹ reporting observations on 126 patients, a skin triangle for use in diagnosis was described. At this time proof seemed at hand that skin tenderness limited to the triangle constituted the most important single sign or symptom of acute appendicitis. Such a deduction was too drastic to be reported on the basis of so small a series of cases and it remained for a more extended period of observation to determine the accuracy of this conclusion. The present article constitutes the more extended study.

SIGNIFICANCE OF EARLY WORK

The subject of cutaneous hyperesthesia is not new. Much research and investigation have been concluded in this field, yet scarcely a reference to skin tenderness is found in textbooks dealing with acute appendicitis. It must be concluded either that this work has been largely overlooked or that it has been examined and rejected. A brief historical review is essential to a thorough understanding of the present interpretation of the subject and also makes it clear why there has been little practical use made of these researches.

The Hypothesis of Ross.—It had long been known that remote areas of skin became tender during the course of certain visceral disorders, a classical example being the writings of Hunter,² who reported a persistent tenderness of his left arm after an attack of angina pectoris. Yet

* From the Third Surgical Division of Bellevue Hospital, service of Dr. George David Stewart, and the Department of Experimental Surgery, New York University and Bellevue Hospital Medical College.

1. Livingston, E. M.: The Skin Signs or Viscerosensory Phenomena in Acute Appendicitis, *Arch. Surg.* 1:83-95 (July) 1923.

2. MacKenzie, James: *Angina Pectoris*, Oxford Medical Publications, London, Frowde, Hodder and Stoughton, 1923, p. 53.

Ross was the first to offer a scientific explanation of this occurrence. His interpretation,³ published in 1888, has become known as the theory of referred pain. Although working at a time when the vegetative nervous system was little understood, he was able to show that nerve fibers pass from the internal organs to the spinal cord and are there associated with sensory nerves coming from the skin. He stated as his belief that this association of fibers within the spinal cord made possible the tender areas of skin already noted.

MacKenzie's Study of Cord Segments.—In 1892 MacKenzie⁴ reported his agreement with the "hypothesis of Ross" and cited many cases explained by this theory. He attempted further to define with accuracy the relation between the spinal segments and the skin. By studying cases of herpes zoster and of diseases of the spinal cord MacKenzie was able to map out areas of skin associated with each spinal segment.

Head Zones.—In the same year Head⁵ published his first paper on identical lines. Through exhaustive researches he was able to map the entire body and limbs into skin zones, each of which corresponded to the cutaneous distribution of pain fibers from one segment of the spinal cord. Head's name has become attached to the theory of referred pain and the study of cord segments, almost to the exclusion of those of Ross and MacKenzie. The skin areas have become known as Head zones. These zones have been greatly misunderstood. Head stated that such zones were not of equal importance in visceral disease, and that he had seen only certain areas thus involved, while in many others he had never encountered such hyperesthesia from internal disorders.

Head's Maximal Points.—This author carefully pointed out that complete zones were seldom to be found in clinical tests. They are theoretical and are determined only experimentally. He taught that these zones all contain maximal points where the skin tenderness is greatest. When hyperesthesia is present in a zone, it may be found only at the maximal point. At times it occurs over a wider area, but seldom throughout the entire zone. In spite of these teachings, the textbooks of the period soon printed Head's charts and represented each zone as being intimately associated with some internal organ. Each viscus was shown to have a "skin representative" for use in diagnosis, and it was intimated that in a disease of such an organ, hyperesthesia was present neatly distributed over the zone indicated. This undue

3. Ross, James, quoted by MacKenzie (footnote 2, p. 18).

4. MacKenzie, James: Associated Pain of Visceral Disease, *M. Chronicle* 16: 295, 1892.

5. Head, Henry: A Disturbance of Sensation, with Special Reference to Pain of Visceral Disease, *Brain* 16:1-122, 1892.

Most recently Cope⁹ of Great Britain made a study of skin signs in appendicitis and found such hyperesthesia in 50 per cent of his cases. However, he likewise described tenderness extending over wide areas, and concluded that "increased cutaneous sensibility must not be taken

6. Healy, Henry. — *Proc. Quacch. Medical Dictionary*, vol. 3.

7. Sherrin. — On the Occurrence and Significance of Cutaneous Hyperalgesia in Appendicitis, *Lancet* 2:186-211 (Sept. 1901) 190-191.

8. Robinson. — The Clinical Bearing of Cutaneous Tenderness in Various Acute Abdominal Disorders, Especially Appendicitis, *Quart. J. Med.* 1:387-416, 1908.

9. Cope, Zachary. — *Clinical Researches in Acute Abdominal Disease*, Oxford Medical Publications, London, Oxford Press, 1925.

by itself to prove the existence of any particular disease" since "various disorders are accompanied by a similar hyperesthesia." Cope, and all previous writers, have approached the subject from a different angle from that of this article. It has been their stated purpose to observe and record all hyperesthesia present in any case later proved one of appendicitis; ours to determine what of this hyperesthesia can be used for diagnosis, to test the utility of a limited area, and to regard as negative all hyperesthesia of wider extent. Former work, then, has described many overlapping skin areas, identical in various disorders and of little practical value.

Twenty years have passed since the publication of Sherren's article. During this period nothing has appeared to alter his conclusions. Since hyperesthesia was believed to be present in so small a percentage of cases, to occur in any of seven different skin areas, and was presented by its investigators as of slight value in the diagnosis of appendicitis, it is small wonder that little reference to the subject is found in current literature.

ADDITIONAL SIGNIFICANCE OF RECENT WORK

The present study assigns an entirely new practical value to cutaneous hyperesthesia in acute appendicitis. This new significance depends on two points of difference from former work; namely, a different method of testing and a different method of localization.

Method of Testing.—Too much emphasis cannot be placed on the necessity of using vigorous tests in eliciting skin signs. This view has not been previously stressed. On the contrary, it was formerly emphasized that vigorous tests should be avoided. The methods previously recommended were the gentle use of a pinpoint or cottonwool dragged across the skin. Sherren stated that "all pressure upon deep structures must be avoided" and advised stroking the skin gently. Robinson wrote, "The best method is to pinch the skin very lightly or to stroke it with a common pin" and that "it is obviously essential that pressure shall be exerted upon no structure other than the skin." These authors found positive skin signs in but 20 to 30 per cent of their cases. Our own tests by similar methods have also shown skin signs to be present in no more than one-fourth of patients with acute appendicitis. Such examinations are totally inadequate. Vigorous tests, on the other hand, show positive hyperesthesia in 86 per cent of cases. It is our experience that the percentage of positive cases is in direct proportion to the grade of stimulus employed.

Traction Test.—We have come to rely almost exclusively on what might be termed the traction method of testing. The skin is picked up between the thumb and forefinger and pulled directly away from the abdomen. A noninvolved area is selected for this initial pull. Traction

is continued outward until the patient signifies discomfort. As a rule a vigorous pull is necessary and is steadily increased until the skin is stretched outward to a marked degree (fig. 1). The amount of force necessary to cause discomfort will vary with different patients. This initial degree of traction is then used as the standard of intensity for that particular patient and uncomfortable pulls of an identical strength are used in all quadrants of the abdomen. In this way any hyperesthetic

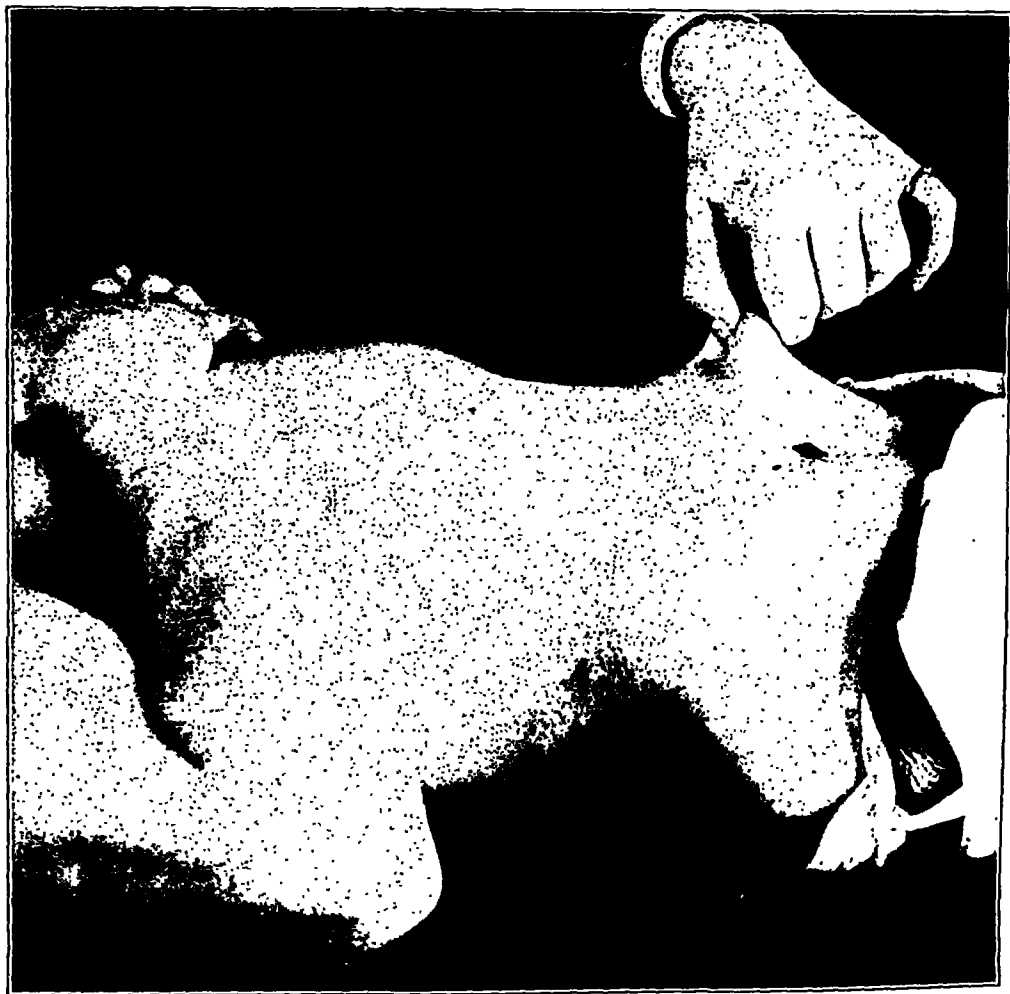


Fig. 1.—Traction method of making sensory test, illustrating the adequate stimulus.

area is readily mapped out. The response within the involved zone is that of real pain and leaves no doubt in the mind of either the examiner or the patient that one area differs from all others. It is utilizing strong tests that makes skin signs so objective and apparent and so greatly increases their value.

A pinch test consists of using vigorous twisting pinches on all parts of the abdominal skin, the pinch being of a degree slightly

uncomfortable even on normal skin. The identical stimulus within an involved zone gives rise to an immediate defensive response on the part of the patient, who winces, cries out or reaches for the examining hand. Tests with heat and cold are refinements that may be of aid in defining the limits of hyperesthesia or in demonstrating the complete sensory change within the involved zone.

Localization.—A generalized skin tenderness can have no specific value. Just as a boardlike rigidity of the entire abdomen gives no indication of the site of an intraperitoneal disease, so a generalized hyperesthesia has no localizing value. All viscerosensory phenomena are produced over definite nerve pathways and should theoretically, therefore, be specific and exact. The entire subject has been confusing through a lack of precision as to localization. One of the questions not yet satisfactorily settled is just what organs can produce skin tenderness and which cannot, and to explain this variation. Another is to define the limits of such cutaneous hyperesthesia originating from a single organ. The ideal method of settling these questions would be through direct experimentation. In the case of the ureter this is readily possible. It has previously been demonstrated¹⁰ that the passage of a ureteral catheter, causing an artificial renal colic, produces skin tenderness on the inner side of the thigh. This hyperesthesia can be produced repeatedly and at will and occurs within a single area, the limits of which are constant. Such data are exceedingly convincing.

Appendicostomy Experiment.—Observations on a patient with an appendicostomy gave similar direct experimental evidence with regard to the appendix. A large bougie, passed into the appendix uniformly, set up a colicky pain and gave rise to a sharply localized cutaneous hyperesthesia. The skin tenderness was always maximal at the center of the appendix triangle and never extended beyond its limits. That this single area has a definite relation to disturbances within the appendix has been tested over an extended period of clinical observation.

The Skin Triangle of Appendicitis.—By the appendix triangle (fig. 2) we mean an area bounded as follows: A line from the umbilicus to the highest point on the right iliac crest forms the upper side; a line carried from this point to the right pubic spine forms its lower side, while a line from the right pubic spine to the umbilicus closes the triangle. These lines coincide with no nerve distribution and the triangle is based entirely on clinical observation. Each of its three boundaries marks a border of use in differential diagnosis. Beneath the lower boundary is that definite area involved by renal colic; above its upper boundary a similar area involved in biliary colic, etc.

Skin tenderness in any of these areas begins at a single maximal point, but in certain instances spreads widely over the abdomen. To be utilized for diagnosis, therefore, arbitrary limits must be established; thus, all overlapping and confusion are avoided. The appendix triangle does not signify either the complete or the sole skin area ever involved in cases with appendicitis; it does signify an area of clinical limits, and hyperesthesia confined to these borders is caused, in our experience, by

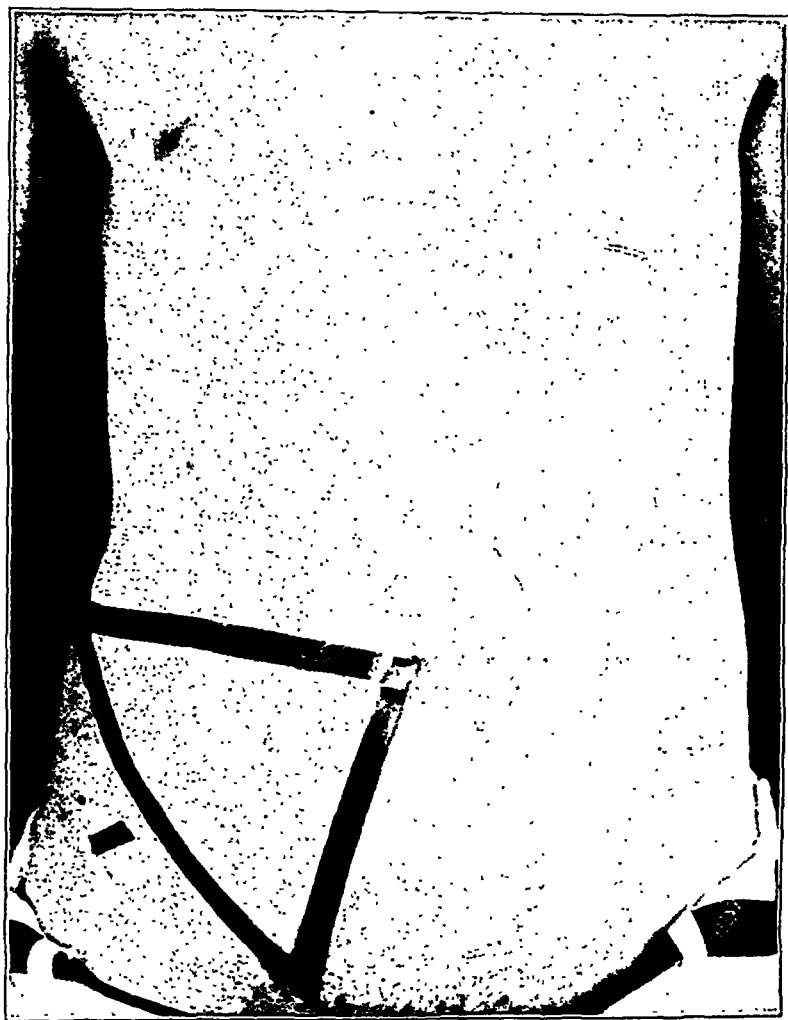


Fig. 2.—Appendix skin triangle: cutaneous hyperesthesia is of aid in the diagnosis of appendicitis only when it is maximal at the center of this triangle and does not extend beyond its limits.

no other intra-abdominal condition than involvement of the appendix. By "positive skin signs for appendicitis" we refer to hyperesthesia, present on the anterior abdominal wall, confined to the appendix triangle, and maximal at its center.

Contrast with Former Work.—While the present study is based on the clinical importance of a single area, former work described many

areas. The seven appendix regions observed by Sherren and Robinson and the regions described by Cope extended to the right hypochondrium, the lumbar region and even to the left side. This wide variation is due to three factors: 1. Light methods of testing give more varied results. 2. In five of the seven areas the hyperesthesia was centered at McBurney's point and fell within the limits of the present triangle. Yet no mention was made of this uniform central point and each region received equal emphasis. 3. In describing hyperesthesia extending over wide areas and well beyond the limits of the triangle, these authors did not differentiate a simple appendicitis from one with complications, such as general peritonitis, the secondary involvement of other organs, or the concomitant existence of two diseases. All skin tenderness encountered in any case was mapped out as an appendix area.

To avoid confusion it seems essential at this point to note the fact that one of Sherren's five areas was a triangle, the limits of which did not vary greatly from our present skin triangle for appendicitis. That this present triangle was worked out without any knowledge of previous work is a matter of little interest. Yet it insures certain fundamental differences. Sherren's triangle was an actual zone of hyperesthesia and was found by superficial sensory tests; it was present in 10 per cent of cases and one of five areas of equal importance, and was not stressed by any subsequent writer. The present triangle, on the other hand, differs in its boundaries, method of elicitation and significance; it is found in 86 per cent of cases, and by both experimental and clinical proof seems to map out the limits of skin tenderness that signify an uncomplicated appendicitis. Our purpose is not in any way to detract from the classical work of Sherren, yet we believe that to refer to the present area as the Sherren triangle for appendicitis is as erroneous as to refer to a Head zone of appendicitis. Sherren himself neither held nor forecast the present interpretation of the subject, neither did he emphasize a triangle to the exclusion of various other widespread skin fields. We give this matter emphasis only to avoid confusion from a similarity of terminology and location between the two areas.

A fundamental justification for the present appendix triangle is found by reverting to the original work of Head. The entire emphasis of this author was on the existence of maximal points of tenderness and on definite limits. The triangle takes cognizance of these points. The triangle forms a basis for a more exact use of cutaneous hyperesthesia. It necessitates the use of a single area in diagnosis, and considers all skin tenderness extending into this area from without, or extending beyond its limits from within, as negative in the diagnosis of appendicitis.

Bellevue Cases.—This method of testing for cutaneous hyperesthesia and this method of localization have been a routine procedure in the Third Surgical Division of Bellevue Hospital since 1921. It is exceedingly important in the interpretation of results to bear in mind that the findings reported are not those of a single investigator or of a group making a special study. More than sixty different signatures appear on these records, the sensory tests being made by attending surgeons, interns and student clerks, and no single signature is encountered in more than forty cases, while the author's appears in only fourteen instances. The figures, then, represent the practical use of the appendix triangle, and its importance relative to other diagnostic data of appendicitis, as obtained in the routines of a large surgical unit.

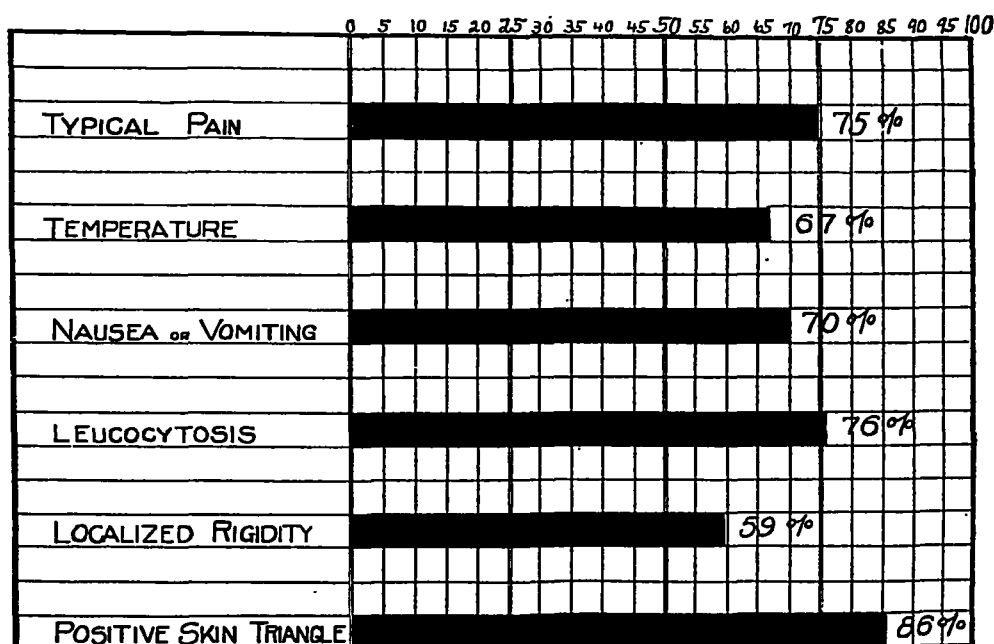


Fig. 3.—Relative frequency of diagnostic data.

Results.—During the 6½ year period covered in this review, March, 1919, to September, 1925, 428 patients with acute appendicitis were admitted to the division. Of these sixty-one are omitted from this report—fourteen had no operations, and the remaining had no tests recorded. In 367 cases with complete preoperative records, the diagnosis of acute appendicitis was confirmed. As in previous publications, a chart has been prepared (fig. 3) showing the relative frequency of the data on which the diagnosis was based. The frequency of each of the classical signs and symptoms in the 367 cases was as follows: typical pain, 286 (75 per cent); nausea or vomiting, 268 (70 per cent); temperature, 246 (67 per cent); localized rigidity, 220 (59 per cent); leukocytosis, 289 (76 per cent). Positive cutaneous hyperesthesia

limited to the appendix triangle was present in 317 instances (86 per cent). In all instances in which the skin signs were negative, a perforative or gangrenous appendicitis was found. Six individual charts, each covering a period of one year, show that the relative frequency of these signs and symptoms remains approximately the same.

These results substantiate all conclusions previously reported from a much smaller number of records. In addition, it is found that this triangle is more frequently present than any other sign or symptom of acute appendicitis.

Certain questions naturally arise in accepting these results: among them, (1) Is this sign pathognomonic of appendicitis, or can it be produced by other conditions? (2) Why is it absent in certain cases of appendicitis? (3) Why should this sign prove to be more reliable than other signs of acute appendicitis?

Not a Pathognomonic Sign.—Positive signs limited to the skin triangle have always, in our experience, signified some involvement of the appendix. This involvement might be classified as follows: (a) acute appendicitis; (b) appendiceal colic, and (c) secondary involvement of the appendix.

Acute Appendicitis.—The conclusion of Sherren that "cutaneous hyperalgesia is probably present at some time during all first attacks of appendicitis" is substantiated by the findings in the present study. Skin tenderness is, however, not always present at a single examination. The hyperesthesia depends on the integrity of certain nerve pathways and destruction of any portion of the nerve mechanism abolishes the sign. Such destruction may be local, focal or central. With necrosis of the appendix the sign disappears (a focal cause): large doses of morphine prior to the examination may mask it (a central cause), and a burn or skin disease within the triangle renders the sign unreliable (a local cause). Barring interruptions of the nerve pathways, cutaneous hyperesthesia is uniformly present during the attack.

The absence of the skin triangle in cases suspected of being acute appendicitis is of almost equal importance. In a previously reported series of sixty operations on patients clinically diagnosed as having acute appendicitis, eleven with negative skin signs (18 per cent) were found to have some other condition such as tubo-ovarian disease, acute nephrolithiasis, pulmonary tuberculosis, etc. Negative skin signs constitute grounds for unusual care. Unless perforation or gangrene of the appendix is present, it is probable that some other disease causes the symptoms.

Appendiceal Colic.—Appendiceal colic will occasionally produce definite localized cutaneous hyperesthesia in patients having no inflammatory condition. A few patients have come under observation, having

abdominal pain and a tender skin triangle but no fever, leukocytosis or other evidence of inflammation. In these cases the symptoms were transient and no operation was performed. It has already been demonstrated by catheterization of the ureter and passing a bougie into an appendicostomy wound that colic without inflammation can produce viscerosensory phenomena. A tender appendix triangle, then, is no criterion for operation and this sign is to be carefully correlated with other diagnostic data.

Secondary Involvement of the Appendix.—In certain instances in which this sign was positive, operation has revealed the primary pathology to be present in some adjacent organ. In all such cases, however, the appendix also was definitely involved. For example, a tubo-ovarian mass with attachment to the appendix may eventually produce skin signs limited to the appendix area. A similar condition might follow the extension into the appendix of an ulcerative enteritis. Neither tubo-ovarian disease alone nor enteritis alone nor any similar condition without simultaneous involvement of the appendix can, according to our experience, produce skin tenderness limited to the area within the appendix triangle described. It seems anatomically possible that other portions of the intestinal tract, having a similar nerve supply, should give rise to skin tenderness and that this hyperesthesia would be limited to the area described, but in commenting on this very possibility Sherren wrote, "I have examined all the cases of abdominal disease which have come under my care at the London Hospital, and have never met with cutaneous hyperalgesia in other diseases of the intestinal tract from the duodenum downward." Our observations have been identical. No case has been observed in which the appendix triangle alone was hyperesthetic yet operation revealed an inflammation of some other abdominal organ, but no appendicitis.

Theoretical Considerations.—We are aware that this sign might theoretically be due to conditions other than appendiceal involvement. For example, a case of herpes zoster of the tenth or eleventh right thoracic roots or a tuberculosis of the spine with pressure on these segments might conceivably be responsible for similar skin tenderness. No such case has come under our observation. The one instance in which it was suspected that such a condition existed was that of a girl having Pott's disease and recent abdominal pain, together with skin signs limited to the appendix triangle (case 276). Operation was delayed twenty-four hours on the assumption that the abdominal signs were due to the spinal disease, yet a subsequent laparotomy revealed a suppurative appendicitis. Were a case of this theoretical type encountered, the complete examination of the patient and the correlation of all data should leave little doubt as to the diagnosis.

In conclusion, it is to be understood that this skin tenderness limited to the appendix triangle does not represent an infallible sign. It may be absent in certain cases with appendicitis (appendiceal perforation), and in certain rare instances it may be present when no inflammation of the appendix exists (appendiceal colic, herpes). To prevent its application in any blind fashion, the factors that render this sign fallible have been stressed at some length. Yet few, indeed, are the instances in which this sign fails to indicate an acute inflammatory condition within the vermiform appendix.

Most Reliable Evidence of Appendicitis.—There seems to be no 100 per cent in physical diagnosis and the importance of various diagnostic methods is relative. On this relative basis our records show that cutaneous hyperesthesia, elicited and localized as here described, deserves a high rating as a diagnostic aid. It is possible, without exceeding the bounds of brevity, to indicate certain reasons why this sign has proved more reliable than any other sign of acute appendicitis.

Pain.—The following in its entirety is quoted from the classic work of Murphy:¹¹

In not a single case is pain absent as an initial symptom. The primary pain with a free appendix is always referred to the epigastrium. The secondary pain is usually not colicky but of the typical inflammatory type and due to periappendiceal involvements. The pain in appendicitis may be referred to the various quadrants of the abdomen, depending on the change in the position of the appendix, either from a congenital or inflammatory malposition. The pain is often referred to the gallbladder region, to the epigastrium, the umbilicus, rectum or chest.

A typical pain, originating at the umbilicus and localizing in the right lower quadrant greatly simplifies the diagnosis of acute appendicitis, yet is present in less than 75 per cent of cases. In the remaining 25 per cent the pain may simulate any known abdominal condition and introduces the greatest element of confusion.

In contrast, the tender skin triangle does not vary in location. Being dependent on a nerve pathway settled in embryologic life it is constant without regard to malpositions of the appendix. It is both an early and a late sign. It is present when the pain is still umbilical in location and outlasts all other signs, forming a definite physical finding of greater value than any vague pain history. Being an objective finding it is independent of the language or intelligence of the patient. This skin tenderness was found in all cases except those with gangrene or perforation, being present in 86 per cent of the series.

Abdominal Tenderness.—Of abdominal sensitiveness Murphy writes, "It is circumscribed in the area of the appendix, whether it be

11. Murphy, J. B.: *Surgery of the Appendix Vermiformis*, Keen's Surgery, Philadelphia, W. B. Saunders Company, 4:750, 1908.

McBurney's point, in the subhepatic space, or in the pelvis." This is not to be confused with cutaneous hyperesthesia. The former signifies an early localized peritonitis; the latter a viscerosensory nerve phenomenon devoid of the variations of site characterizing point tenderness.

Nausea and Vomiting.—These were observed in only 70 per cent of cases, actual vomiting in a far lower percentage of cases. As it occurs in most acute abdominal conditions, the value of vomiting as a single sign of appendicitis is slight. As a part of the classical picture of appendicitis, when present, it has considerable value; the absence of vomiting is not even presumptive proof of absence of appendicitis.

Temperature.—Elevated temperature was observed in only 67 per cent of the hospital cases. It varies exceedingly during an attack. In many cases with a retroperitoneal appendix or a fulminating appendicitis it is absent during the entire period of observation. Its presence in typhoid fever, pneumonia, pleurisy, influenza, cholecystitis, salpingitis and other diseases giving acute abdominal symptoms scarcely needs mention.

Leukocytosis.—This is considered by most authors as merely of corroborative value. It was present in 76 per cent of cases. Leukocytic counts are subject to technical error, are often the cause of great delay, and by no means uniformly show elevation. Blood counts have a unique value in determining a suppurative peritonitis following perforation or gangrene of the appendix when pain, skin tenderness, temperature and rigidity may or may not be present. Counts should be made in every case of suspected appendicitis, yet are often not made at the time when most needed. The evidence from skin signs is immediately available at the first bedside examination.

Rigidity.—This sign, being dependent on definite nerve pathways, should theoretically be analogous in value to skin tenderness. To detect an early localized rigidity is, however, an art. Furthermore, rigidity varies with the site of the inflammation; may be absent in some cases of appendicitis, notably the retroperitoneal type, and in the majority of instances, when present, soon becomes generalized, thus losing its value as to localization. Localized rigidity was present in fewer instances than any other classical sign, being observed in 59 per cent of the series. An invaluable index pointing toward a surgical condition within the abdomen, its value as a single sign of appendicitis is inferior to that of cutaneous hyperesthesia, the history, deep tenderness and other diagnostic data.

That cutaneous hyperesthesia limited to the skin triangle was found to be the most valuable single sign of acute appendicitis may be considered due, in part, to its precise localization, explained on embryologic, anatomic and physiologic grounds; to its early occurrence in the course

of the disease; its persistence after other signs have subsided; to the objective nature of the sign; to its experimental proof, through appendicostomy tests, and to its clinical proof through the extended study of an impartial group of observers. The routine use of the skin triangle for appendicitis promises to introduce an element of greater certainty into the diagnosis of this common disease.

CONCLUSIONS

1. Although the study of cutaneous hyperesthesia in appendicitis is not new, skin tenderness has previously been considered of slight use in diagnosis.

2. Recent work assigns an entirely new practical value to skin signs.

3. This is based on (*a*) a new method of testing and (*b*) a new method of localization.

4. Strong grades of stimuli are necessary in eliciting skin signs.

5. The hyperesthesia of use for diagnosis is limited to a skin triangle which has been mapped out through clinical observation and appendicostomy experiments.

6. This sign was present in 86 per cent of over 400 patients with acute appendicitis.

7. In the present study, this sign, of positive cutaneous hyperesthesia limited to the appendix skin triangle, was found to be of more value than any other sign or symptom in the diagnosis of acute appendicitis.

INTRAPELVIC ECTOPIC TESTIS COMBINED WITH ECTOPIA VESICAE, CONGENITAL UMBILICAL HERNIA AND ABNORMAL GALLBLADDER

A RARE CASE *

H. A. HARRIS, M.B., B.S.

ST. LOUIS

A primipara, who reported no unusual history, gave birth to a male infant with extopia vesicae and a large umbilical hernia. The child died on the twenty-seventh day of inanition and bronchopneumonia. At necropsy the infant was markedly wasted, and there was a large tumor extending from the umbilical scar cranially to the epispadic glans penis caudally. The tumor was the size of a grapefruit and in its upper three-quarters was covered with thin skin and distended by coils of intestines. The lower portion of the tumor presented a dark red mass that was the posterior wall of the extroverted bladder from which urine had dribbled continuously. Between the area of thin skin and the area of bladder mucous membrane was a narrow crescentic zone of pinkish epithelium that showed a fine wartlike proliferation and excoriation. The left testis was visible as a subcutaneous swelling in the groin, but there was no trace of the right testis on inspection or palpation; the right scrotal sac was not formed.

A roentgenogram of the cadaver (fig. 1) displayed marked gastroschisis, the two pubic bones being separated by a very wide interval, as the left pubic bone lay anterior to the hip joint and the right pubic bone lay lateral to the right hip joint. Both bones had undergone rotation as well as lateral displacement. The ischia were also separated to a marked extent so as to give a roomy pelvis.

The thorax displayed a marked shrinkage of the thymus gland; the maximum length thereof was 1 cm. and the width 0.5 cm. Extensive areas of bronchopneumonia were seen in the lungs. The heart was normal from the anatomic point of view and the ductus arteriosus was completely closed. The abdomen was opened by an incision along the costal margins and midaxillary lines so that a large flap of abdominal wall could be turned down. The coils of intestine were disposed on either side of a long drawn out mesentery which ran from the great curvature of the stomach to the ringlike opening of the umbilical sac. To the right of this mesentery were arranged coils of ileum and to the left was the colon. The umbilical opening was 4 cm. in diameter and

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was limited on either side by the obliterated umbilical arteries which ran to the umbilical scar at the cranial margin of the umbilical ring. The distended coils of intestine were with difficulty dislodged from the sac, and there was no trace of adhesive peritonitis, but the mesentery was fused with the wall of the sac in the angle formed by the fusion of the umbilical arteries. There was no trace of a Meckel's diverticulum or of vitelline arteries. On careful examination the mesentery above described as extending from the great curvature of the stomach to the sac was seen to be continued along the ascending colon to the cecum and appendix, which occupied the most distal portion of the sac. When this was displaced to the left, the mesentery of the small intestine was seen to be continued within the sac with its contained branches of the superior mesenteric artery. Approximately one half of the ileum and one third of the colon occupied the sac (fig. 2).

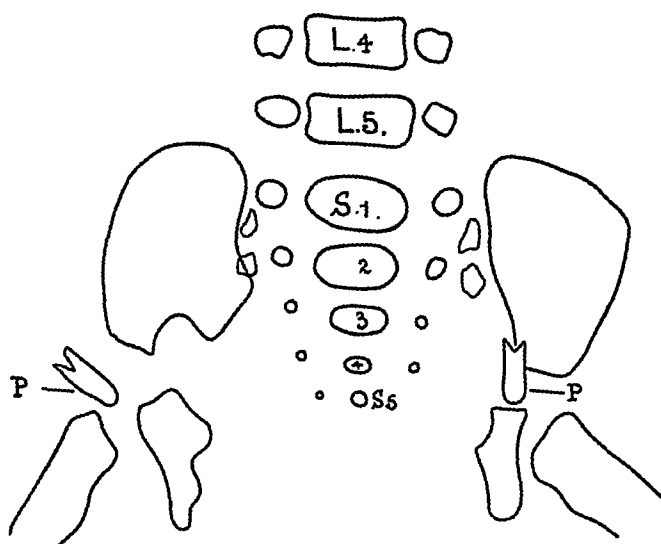


Fig. 1.—Diagram of roentgenogram of pelvis showing displacement and rotation of pubic bones, P.

The stomach and pylorus were normal in position but the duodenum was disposed entirely to the right of the middle line. The third part of the duodenum and duodenojejunal flexure were situated anterior to the hilum of the right kidney. The jejunum and the proximal portion of the ileum lay in the right upper quadrant and right lower quadrant of the abdomen, and the distal portion of the ileum was in the hernial sac. The common bile duct held the normal relation to the first part of the duodenum, but entered the posterior aspect of the duodenum at the junction of the first horizontal part with the second vertical part. The gallbladder was abnormal as regards shape, position and attachments. From a normally formed porta hepatis the bile duct ran downward to the point of divergence of the common bile duct and cystic ducts. The

cystic duct passed to the right and then made a hairpin bend whereby the gallbladder was displaced from the normal fossa and occupied a horizontal position behind the falciform ligament with its fundus 2 cm. to the left of the middle line, between the anterior aspect of the stomach and the left lobe of the liver (fig. 2). The terminal portion of the cystic duct and the proximal portion of the gallbladder were attached

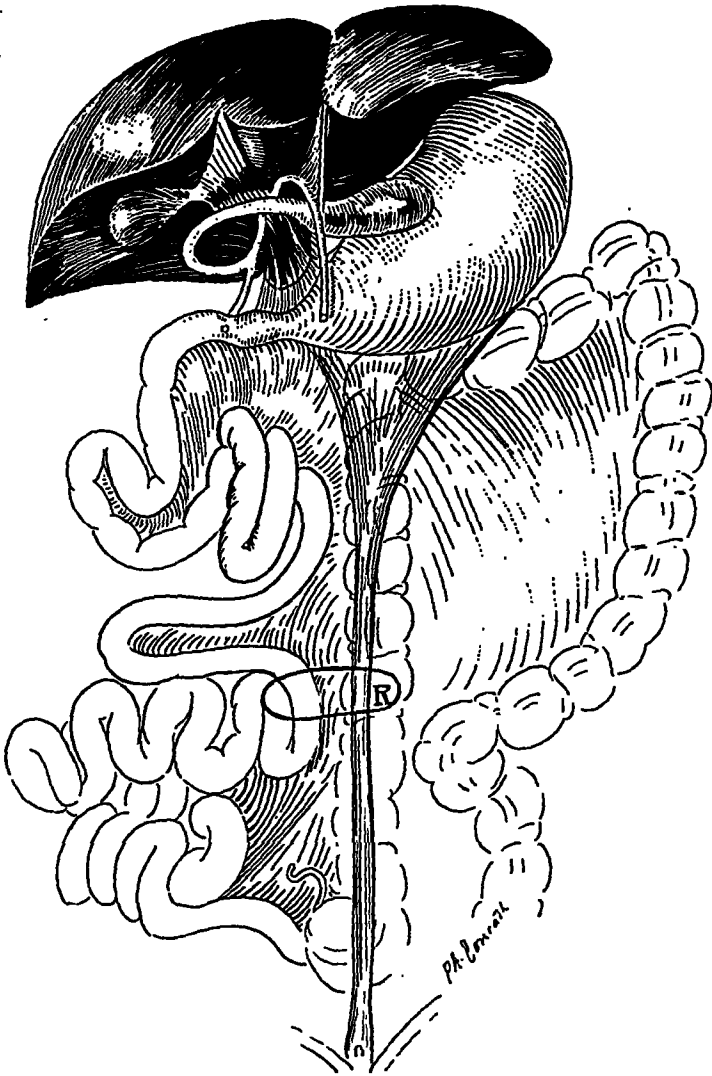


Fig. 2.—Dissection of the contents of the abdomen and hernial sac, the neck of which is marked by a circle at *R*.

by a mesentery to the site of the normal fossa for the gallbladder. This fossa had a deep fissure which coursed downward and forward to cut the inferior margin of the liver 2.5 cm. to the right of the falciform ligament. To the right of this fissure was an accessory lobe of the liver which was biconvex in shape and suspended by its margin from the lateral lip of the fissure, no mesentery intervening.

The portion of the colon proximal to the neck of the sac was separated from the pyloric vestibule by a distance of 3 cm. which was bridged across by a "duodenocolic" ligament which had maintained the colic angle in close relationship to the pylorus and first part of the duodenum. From this colic angle the colon passed to the left to form a well marked splenic flexure in relation to the sustentaculum lienis. The descending colon lay anterolateral to the left kidney, and its mesentery was so well developed that a large peritoneal fossa lay between the

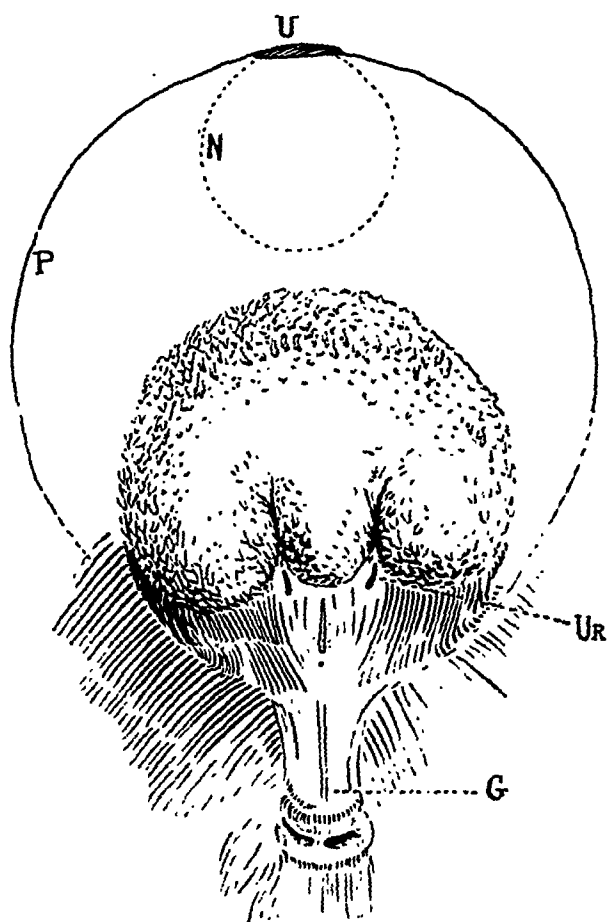


Fig. 3.—Ectopia vesicae: *U*, umbilicus; *N*, neck of sac; *P*, periphery of sac; *Ur*, ureter, and *G*, glans penis with epispadias.

mesocolon and left colic branch of the inferior mesenteric artery anteriorly and the left kidney posteriorly. The sigmoid colon was of average length, had a well marked mesentery, and lay almost entirely in the true pelvis.

The bladder displayed the typical features of ectopia vesicae and epispadias, the openings of the ureters, ejaculatory ducts and prostatic ducts presenting no marked departure from the classical description (fig. 3).

The right testis was situated in the true pelvis at the site of the normal adult ovarian fossa. The testicular vessels coursed downward over the brim of the true pelvis crossing the external iliac artery to the ureter and coming to lie to the inner side thereof—a position closely resembling that of the infundibulo-pelvic ligament in the



Fig. 4.—The ectopic intrapelvic testis on the right side; *V. D.*, vas deferens; *V. S.*, seminal vesicles; *U.*, ureter, and *T. V.*, testicular vessels.

female. In the illustration (fig. 4) the testis is raised out of the pelvis in order to show its attachments. The true caudal pole was superior and lateral and the true cranial pole was medial and inferior. The testicular artery is shown dividing at the true caudal pole. The testis was buried in a fold of peritoneum with a considerable

amount of fat, the caput being inferior and the tail superior; the fat formed a well defined lobule around the caput. The vas deferens lay distal and parallel to the ureter and the seminal vesicle touched its fellow in the midline posterior to the extroverted bladder. The gubernaculum was attached to the caudal pole of the testis at a point that lay slightly medial and inferior to the ureter. This point (fig. 4) is displaced somewhat as the testis had to be raised from the true pelvis in order to bring it into view. From the true caudal pole of the testis a fold of peritoneum spread outward and upward into the false pelvis in front of the gubernaculum and lay between the coils of ileum in the right iliac fossa. The gubernaculum entered the internal abdominal ring and its fibers could be traced to the skin of the groin, to the intramuscular connective tissue of the abdominal muscles, but not to the scrotum or perineum.

UMBILICAL HERNIA AND ECTOPIA VESICAE

Frazer and Robbins¹ have described in detail the various phases of the normal physiologic umbilical hernia which appears in the human embryo at the fourth week and persists to about the thirteenth week. About the tenth week they describe the process of rotation of the intestine which gives to the adult human being its typical conformation as a result of the reentrant coils of small intestine returning before the colon and passing to the left beneath the mesenteric vessels and umbilical colon. Several cases of nonrotation and malrotation have been described in detail by Dott,² who maintains that 'failure of rotation up to this stage occurs in connection with extroversion of the bladder.' The persistence of the colic angle and duodenocolic ligament also characterizes this type of case.

In what manner can the umbilical hernia and ectopia vesicae be correlated? At the beginning of the third month in an embryo of 30 mm. Bryce³ has shown that the pubic bones are represented by two small nodules of cartilage which lie respectively right and left of the pars urethralis of the urogenital sinus (fig. 5). The pubes are characterized by a late appearance in cartilage, slow growth and a late date of ossification at the sixth month. Parallel to this slow growth and differentiation of the pubic bones we have a late differentiation of the wall of the bladder. The first musculature to appear in the wall of the bladder is the longitudinal muscle which appears toward the end of the second month at the 22.5 mm. stage. This layer is always more distinctly developed on the dorsal aspect than on the ventral aspect and may often be entirely

1. Frazer, J. E., and Robbins, R. H.: On the Factors Concerned in Causing Rotation of the Intestine in Man, *J. Anat. & Physiol.* **50**:75-110, 1915-1916.

2. Dott, N. M.: Anomalies of Intestinal Rotation, *Brit. J. Surg.* **11**:251 (Oct.) 1923

3. Bryce, T. H.: Quain's Anatomy, Embryology **1**:196, 1918.

wanting ventrally, according to Felix.⁴ The inner layer of circular musculature appears when the embryo reaches the 26 mm. stage and the internal longitudinal layer, which rapidly assumed an oblique character, does not appear until the 60 mm. stage. This late differentiation of the pubic bones and of the musculature of the bladder is also associated with a late date of formation of the portion of the abdominal wall between the umbilicus and the pubes. The large umbilical opening in the embryo of 20 mm. is of such a size that the two recti are separated by a very wide gap, and the caudal limit of the hernial opening is very near to the cloacal tubercle which is developed into the genital tubercle and phallus. This portion of the anterior abdominal wall is of a short length and lies in a plane that is almost horizontal. At the twelfth week the return of the intestine from the extra-embryonic celom to the abdominal cavity proper, consequent on a relative decrease in the

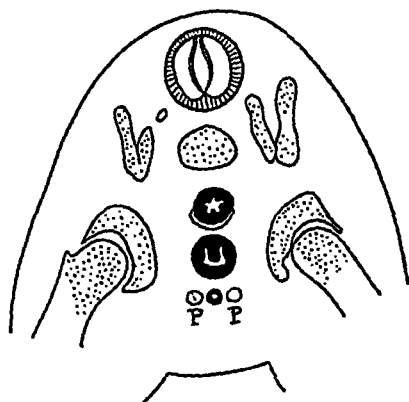


Fig. 5.—Testis of human embryo of 30 mm. at beginning of third month (after T. H. Bryce); the urethra is shown between the pubic cartilages, *P*; posteriorly lie the urogenital sinus and rectum.

rate of growth of the liver,¹ causes a rapid growth in this portion of the anterior abdominal wall and a change in its position from the horizontal to the definitive vertical position. At the same time the recti approach the middle line and rapidly reduce the large opening of the umbilical hernia. The late growth, differentiation and change of position of the lower half of the anterior abdominal wall proceeds very rapidly after the thirteenth week and there are no traces therein of the tendinous lineae transversae which characterize the upper half of the rectus sheath. It is suggested that the delay in the development of the pubes, in the lower half of the anterior abdominal wall and in the musculature of the bladder, is due to the coexistence of the normal physiologic hernia, and that further the return of the intestine to the abdominal cavity is the decisive factor in determining the late but rapid growth and differentiation of these structures.

4. Felix, W.: Keibel an Mall's *Embryology* 2:880, 1912.

THE ECTOPIC TESTIS

Since Hunter described the gubernaculum testis it has been held that the ectopic testis could be found wherever the gubernaculum testis obtained a partial attachment. The gubernaculum may be regarded as a four tailed ribbon with attachments to the interstitial connective tissue of the anterolateral abdominal muscles in the neighborhood of the internal abdominal ring, to the subcutaneous tissue of Scarpa's triangle, to the subcutaneous tissue of the perineum and lastly to the scrotum. In each of these situations the testis may be found. An ectopic testis in the true pelvis, as found in this case, is a rare anomaly and it is difficult to account for its atypical position and attachments. Apparently the testis has descended into the true pelvis not only by an actual internal descent but also by a rotation through an angle of 180 degrees about an anterioposterior axis whereby the true caudal pole has remained anchored to the gubernaculum while the true cranial pole and caput epididymis have descended into the true pelvis.

Felix, in his account of the external descent of the testis, after stressing the absence of an internal descent, says that the testis is brought away from the posterior abdominal wall to gain attachment to the anterior abdominal wall by the development of two new structures, and this notwithstanding the increase in the sagittal diameter of the body cavity consequent on the return of the umbilical intestine to the body cavity. The first process to form is the *inguinal crest*, an outgrowth of the anterolateral wall of the abdomen, which grows back as a ridgelike fold in the sagittal plane. The second is the *inguinal fold*, a thick fold of the mesonephros, which is covered with a thickened epithelium and filled with a somewhat more compact mesenchyme. The upper third of the inguinal crest lies opposite the inguinal fold; in this upper third of the inguinal crest a thickening of the mesenchyme develops, and spindle shaped cells appear and form bundles that run in a horizontal direction from the crest toward the integument. The inguinal fold and the upper third of the inguinal crest fuse and thereby the connection between the mesonephric fold and the anterior abdominal wall is accomplished at the 26 mm. stage. Thus the testis is connected with the anterior abdominal wall: (1) by its mesorchium or the epigonal portion of the genital fold; (2) by the plica mesonephridica; (3) by the plica inguinalis, and (4) by the crista inguinalis.

Within this fold is formed, in four distinct parts, a cord of compact spindle shaped cells, the chorda gubernaculi of Hunter. This cord is clearly differentiated before the recti have met in the middle line by the rapid growth of the anterior abdominal wall between the umbilicus and the pubes consequent on the return of the intestine and closure of the umbilical hernia. It is suggested that in the present case, the wide

liver is not secondarily displaced into the hernial sac, but is situated there from the first. The so-called "adhesion" of the liver to the wall of the sac is not the result of inflammatory action, but is due to the union of the liver with the abdominal wall, and to the fact that the separation of the two has been imperfect. The primitive liver bud grows forward from the junction of the foregut and yolk sac in the ventral mesentery until it fuses with the septum transversum. At a later stage this fusion or "adhesion" has to be broken down so that the liver is freed from the anterior abdominal wall and from the septum transversum anteriorly and superiorly. In this process of fusion and subsequent breaking away, accessory lobes can be formed and in those cases of persistent umbilical hernia in which the liver becomes involved in the hernia the formation of accessory "traction" lobes will be more marked. Those lobes which have the typical arrangement of four vessels, i. e., hepatic artery and vein, portal vein and bile duct, will tend to persist. If the traction produces obliteration of the lumen of any or all of these vessels, then the accessory lobe will atrophy.

The gallbladder is but rarely seen with a mesentery attached thereto in children. In adults, and in the aged in particular, a short mesentery is sometimes seen; very frequently it is the result of the traction of an overdistended gallbladder or of recurrent attacks of local peritonitis. Jacquemet¹⁰ has described this mesentery and its frequency has been given as varying from 5 per cent to 0.5 per cent of cases. From the point of view of comparative anatomy it is interesting to note that no general principle of development has succeeded in correlating the fissures and lobes of the liver, the attachment of the gallbladder with or without a mesentery and the relative size and development of the various parts of the alimentary canal. His,¹¹ Ingalls,¹² Bradley and Lewis¹³ have studied the influence of the omphalomesenteric and umbilical veins in determining the lobulation of the liver. In particular Mall's¹⁴ description of the primitive six lobules of the liver has been studied, but as yet they have not been shown conclusively to be the equivalent of the six lobes of the typical mammalian liver. It is suggested that the normal change over from a primitive liver bud in association with one or both omphalomesenteric veins to the later fetal liver in association with the umbilical veins and later with the left umbilical vein only, together with the changes

10. Jacquemet, M.: *Considerations sur les anomalies du foie et des voies biliaires*, Thèse de Lyon, 1896.

11. His, W.: *Anatomie menschlicher Embryonen* 1:1-84, 1888.

12. Ingalls, N. W.: A Contribution to the Embryology of the Liver and Vascular System in Man, *Anat. Record* 2:338-344, 1903.

13. Lewis, F. F.: The Development of the Liver, Keibel and Mall's *Embryology* 2:403-428, 1912.

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taking place in the normal physiologic umbilical hernia, may yield the answer to this puzzling question. In persistent cases of umbilical hernia containing portions of liver the persistence of the omphalomesenteric veins has been described. Serial sections of various embryos are at present being studied from this point of view in order to ascertain if the physiologic umbilical hernia in association with the omphalomesenteric-umbilical complex has any effect thereon.

The abnormal position of the fundus of the gallbladder in the case discussed should be noted as a possible cause of an atypical clinical picture. Now that the cholecystographic method of Graham¹⁵ is being extensively used for lesions of the gallbladder, every atypical position of this viscus has acquired an added interest.

CONCLUSION

This infant presented a combination of anomalies characterized by the absence of those associated deformities of early embryonic life which involved the nervous, skeletal and circulatory systems. It is in such a case that we see the value of the conception of the "space-for-time" division of antenatal pathology which we owe to Jonathan Hutchinson and Ballantyne.¹⁶ The life of this individual seems to have been normal during the embryonic period of the first two months. The anomalies crept in during the neofetal period of the third month, leading to persistent umbilical hernia, ectopia vesicae, ectopia testis and minor irregularities of the liver. This period, the third month, is devoted in particular to the definite establishment of the placental regimen and to the surrender of the vitelline circulation. The frequency of abortion during the third month is a well known clinical fact and a failure of effective placental connections is almost certainly associated therewith. For this reason a plea is made for the routine histologic examination of all placentae from abortions of the third month with a view to eliciting the pathology thereof at a time when the activity of the layer of Langhans and of the syncytium is at a maximum.

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THE USE OF FASCIA FOR THE REENFORCEMENT OF RELAXED JOINTS *

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RELAXATIONS OF THE KNEE JOINT

During the last few years serious thought has been given to the treatment of relaxed knee joints and many operations have been developed for the reconstruction of the crucial ligaments, most popular of which are those described by Hey Groves, Smith and Gallie. These procedures have been used with success in the type of disability for which they were designed, namely, the extremely relaxed knee joint, resulting from a complete rupture of one or both crucials plus a general relaxation of the capsule. The disability in these cases is so great that the patient is unable to use the member for the ordinary functions of civil life.

In contrast to this type there exists among young, active athletes a type of relaxed knee that performs the normal functions of civil life but which does not permit the individual to participate in active, rugged athletic pursuits. It is this type of disability to which our attention has been directed and to which the described operation is applicable. The common internal derangement of the knee is usually treated with precision. So much has been written on this subject that the medical profession at large is thoroughly familiar with the signs, symptoms and treatment of injury to the semilunar cartilage, loose bodies, etc.

For a number of years the crucial ligament injuries have been stressed, and exhaustive physiologic and anatomic studies have been made with the result that the actual importance of this ligament has, in a way, been overestimated. It has not been so long ago that we were led to believe that a completely severed crucial ligament was irreparable and resulted in a complete disability of the leg. Careful clinical observations and explorations of the knee have shown that the anterior crucial ligament may be completely severed and yet we will still have a fairly stable knee joint, provided the other ligaments, particularly the internal lateral ligament, are intact.

A stretched, attenuated or torn anterior crucial ligament gives a disability that is troublesome to the athlete. It permits an outward rotation of the tibia and an increase in the abduction of the tibia when the leg is in a semiflexed position. It, therefore, explains the pseudo-

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locking (or slipping out) of the knee of which the athlete complains when he attempts to turn suddenly with the leg slightly flexed and the thigh adducted.

The operation I am going to describe is designed to reenforce the capsule of the joint in a way that will help to sustain the leg when it is in this position and is like a substitute for the anterior crucial ligament.

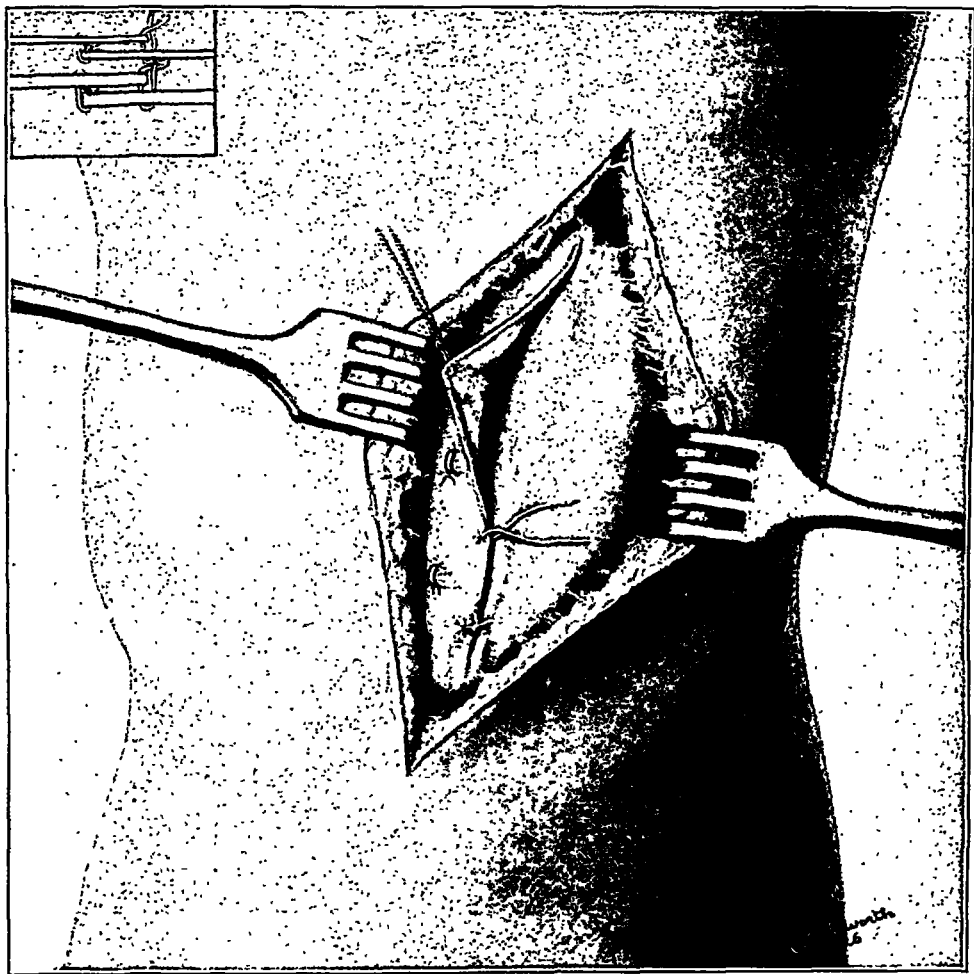


Fig. 1.—Overlapping plication of capsule and fascia.

Briefly stated, the patient gives a history of a major injury of a twisting nature and a total disability for several weeks, following which there is good function and no symptoms except when a sudden strain is put on the leg when it is slightly flexed. The slipping of the knee occurs with an increasing frequency but is not associated with as much disability as with the initial injury. During the last four years we have operated on eight young adults who presented this type of disability. Sufficient time has elapsed in six of the cases to judge the

end-result, the other two being too recent to permit any conclusions. Of the six cases mentioned in this report five have been successful and one a failure.

DESCRIPTION OF OPERATION

An incision is made about three-fourths inch (1.8 cm.) medial to the inner border of the patella, extending downward parallel with the

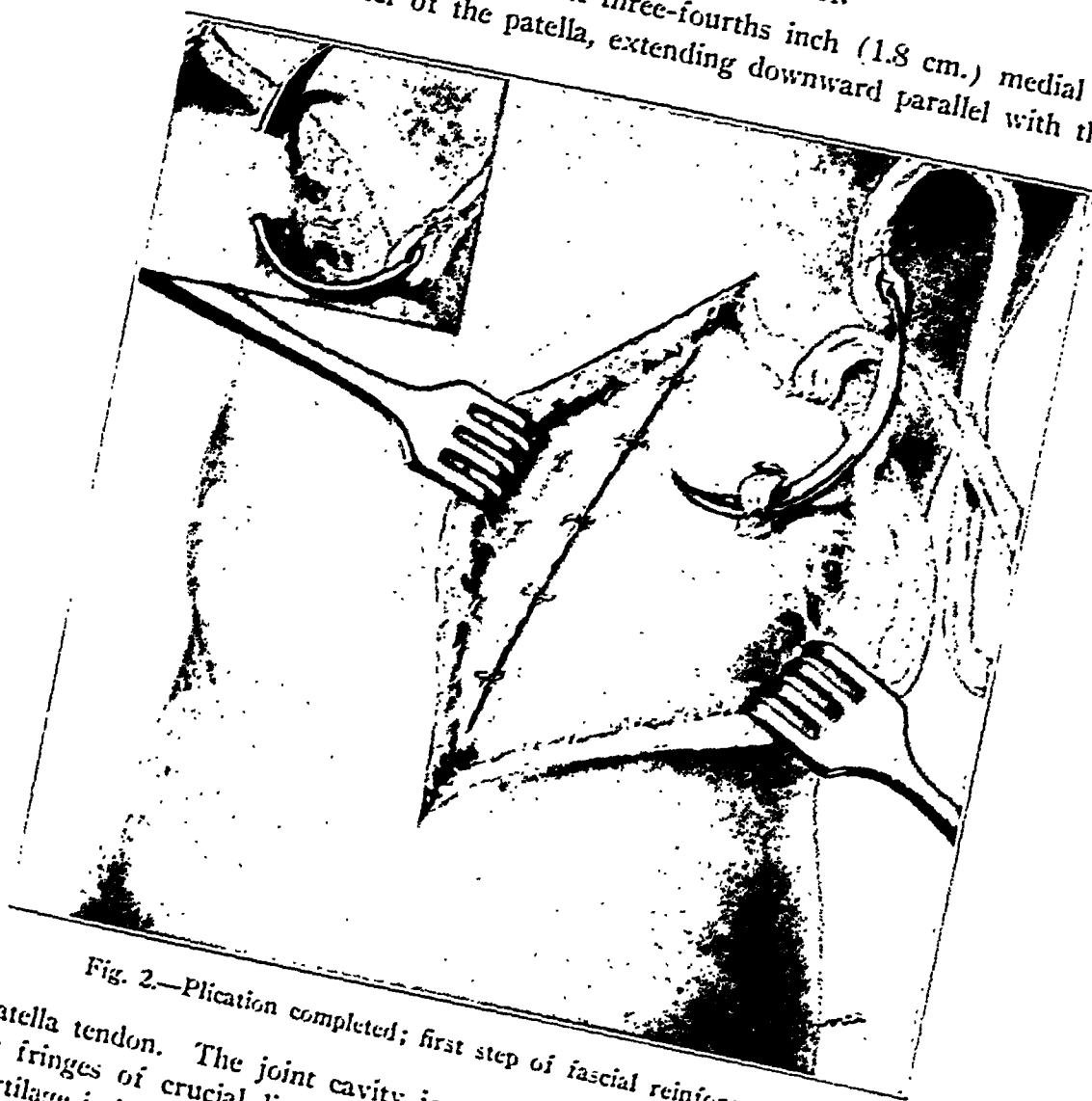


Fig. 2.—Plication completed; first step of fascial reinforcement.

patella tendon. The joint cavity is opened and inspected; any debris or fringes of crucial ligaments are removed; the internal semilunar cartilage is investigated for any possible derangement; closure is made by overlapping the ligamentous structure and drawing the capsule as tightly as mattress sutures will permit. The fascia covering of the capsule is treated by the same overlapping method (figs. 1 and 2). This gives a thick ligament which extends from the inner border of the patella obliquely across the joint. A distinct welt can be felt which seems to persist permanently. In our most recent cases, we have added

strips of fascia to the plication of the capsule reenforcement of the lateral border of the internal lateral ligament, as shown in figure 3. Thus we have reenforced the internal surface of the knee joint in a way that we feel supports the knee when the tibia is in a position of slight abduction and partial flexion. We did not use the patella splitting incision as we wished to use our exploratory incision in the plication.

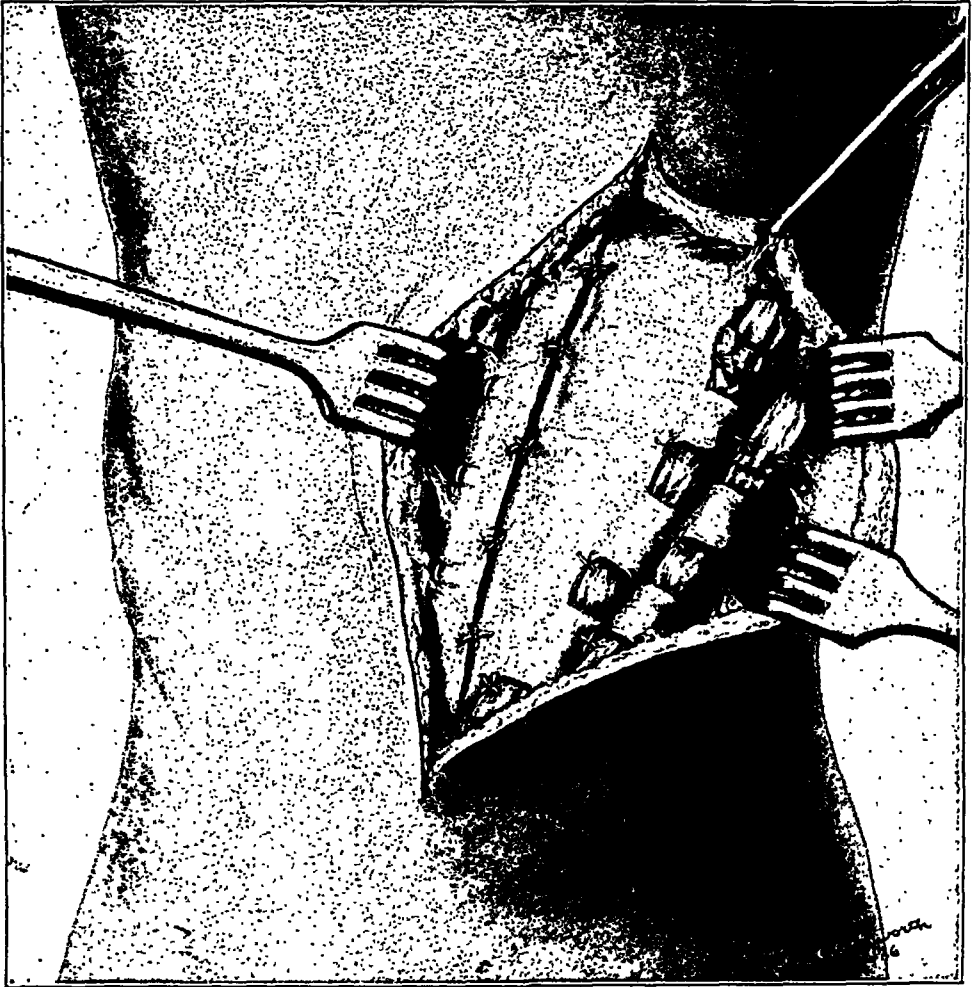


Fig. 3.—Plication and reinforcement completed.

POSTOPERATIVE TREATMENT

From four to six weeks in a plaster-of-paris cast is followed by gradual exercise and development of the quadriceps and the hamstring group of muscles.

REPORT OF CASE

CASE 1.—T. S., a man, aged 26, ten days before examination while playing soccer wrenched the right knee. He was immediately disabled, being unable to extend the knee within 10 degrees of full flexion.

The knee was acutely swollen with an inability to extend it fully. There was no sensitiveness about the internal semilunar cartilage. Exploration of the joint, May 11, 1922, disclosed a torn anterior crucial ligament with frayed pieces wedged between the tibia and the femur, preventing the leg from being fully extended. These were removed. The internal semilunar ligament was normal and therefore was not removed. Closure was made by an overlapping plication of the ligaments and fascia. The leg was immobilized in plaster-of-paris for one month.

In the fall of 1922 this young man was captain of his college soccer team, and was elected a member of the All-American Soccer Team. In 1923 he continued to play soccer and was elected captain of the All-American Soccer Team. There can be no question as to the end-result in this case.

CASE 2.—A. B. S., a man, aged 23, was admitted to the hospital, May 23, 1923. In 1921, while playing football, he suddenly twisted his knee, and this was followed by complete disability. He was unable to continue in football during that year. In 1922 he began to have a continued slipping of the knee joint when attempting to turn or throw any weight on the leg while in a partially flexed or slightly adducted position. As he would express it, his knee would slip out and snap back. There was no locking, but there was considerable pain followed by swelling.

There was no tenderness about the internal semilunar cartilage. There was a moderate relaxation of the knee joint with an ability to slide the tibia forward on the femur. Little increase in lateral motility was noted.

An exploratory operation was performed. The internal semilunar cartilage was normal. The crucial ligament was frayed and stretched, being about one-half its normal size. Several loose pieces of frayed ligament were removed; a plication of the capsule closure was made.

This young man was captain of his college football team and played throughout the entire season of 1923 with no inconvenience so far as his knee was concerned. There can be no question as to the end-result of a functional return in this case.

CASE 3.—J. W., a man, aged 20, was first seen Nov. 8, 1923, giving a history of having sustained a twisting injury to his knee eight months before. This was followed by complete disability, which lasted for about three weeks. After that time he was greatly inconvenienced by the knee slipping when the leg would be in a position of partial flexion and the tibia abducted on the femur. He never had any locking. He was admitted to the hospital, Nov. 11, 1923, and an exploratory incision was made. There was a torn anterior crucial ligament; frayed sections were removed. The internal semilunar cartilage was normal. A plication closure was made. The leg was immobilized in a cast for six weeks following the operation.

We were unable to get a report from this patient at the present time. However, one year after the operation he was able to indulge in athletic exercise and could play basket-ball without any discomfort.

CASE 4.—W. E. M., a man, aged 21, was first seen July 24, 1923, giving a history of having sustained a twisting injury to his knee in 1920. This was followed by complete disability for several weeks. He was unable to play basketball or baseball. He had had continuous trouble of pseudolocking of the knee after that time. Physical examination showed an ability to slide the tibia forward on the femur. An exploratory operation was performed on the knee, Jan. 29, 1924. The anterior crucial ligament was torn. The internal semilunar cartilage was normal, and was not removed. Plication and reenforcement of the lateral ligament were done. The leg was in a plaster cast until March 6, 1925.

The patient reports that last winter he played eighteen games of basket-ball with absolutely no inconvenience to the knee. He is also able to engage in active, rugged exercise, such as baseball.

CASE 5.—B. H. M., a boy, aged 17 years, was first seen Nov. 8, 1924, giving a history of having sustained an injury to his knee two weeks before. Examination showed considerable synovitis with an increase in fluid, tenderness about the internal lateral ligament and marked relaxation of the knee joint. There was a great deal of pain on movement. The leg was immobilized in a position of 15 degrees short of full flexion for a period of four weeks. Following this a knee cage was applied and was used for several months. March 20, 1925, the patient reported that he was unable to engage in athletics, even with the use of the knee cage. Exploration, March 22, 1925, showed a complete rupture of the anterior crucial ligament with a very movable semilunar cartilage. The cartilage and frayed pieces of crucial ligament were removed. The capsule was plicated. The leg was immobilized for a period of four weeks following operation, after which the knee cage was reapplied.

This young man has been unable to engage in his favorite sport of football as the knee still continues to give him trouble. It is interesting to note that this was the case in which the cartilage was removed, and is the only case in which we failed to get a perfectly satisfactory result.

CASE 6.—T. T., a man, aged 21, was first seen after a football injury in the fall of 1921, having sustained a severe wrench of the knee associated with swelling and complete disability. Diagnosis of a torn crucial ligament was made and suitable immobilization was instituted for a period of six weeks, following which a knee cage was applied. With the use of the knee cage the patient was able to play football during the following season. Since that time he had had an increasing disability and slipping of the knee so that he was unable to indulge in any rugged athletics or do the ordinary things of civil life without inconvenience.

Physical examination showed that the patient had an ability to slide the tibia forward on the femur, and a considerable amount of lateral mobility of the knee. An exploratory operation was performed on the knee, June 9, 1925, which showed the anterior crucial ligament to be frayed and relaxed. The cartilage was normal. Plication of the capsule and reinforcement with fascia were done.

The patient reported, April 12, 1926, that he was able to run, play baseball, and was in training as a member of his crew at his university. During the last year he was also able to do fancy dancing without any

inconvenience. There is no evidence of any relaxation of the knee joint at the present time.

We believe that the six cases that we have reported have been done over a sufficient period of time to allow us to judge the end-results, five of the six having been unqualified successes, what seems to be a perfectly normal knee being restored to the athlete. I feel that the procedure is a satisfactory one in well selected cases. I do not advocate the use of this operation until all conservative treatment has failed.

I have also found strips of fascia useful in the repair of radio-ulnar relaxations and recurrent dislocations of the sternoclavicular articulation. The objection to the use of fascia in the latter case is that it produces quite a marked deformity from the mass of soft material and is, therefore, not advisable in female patients in whom personal appearance is to be considered.

RECURRENT DISLOCATION OF THE SHOULDER

There is perhaps no common joint disability that has to its credit more types of operations for its cure than recurrent dislocation of the shoulder. One naturally concludes that the ideal operation has not been described or there would be no need for so many surgical procedures: muscleplasties, capsulorrhaphies, bone grafts and fascial transplants. It is not my desire to review the volumes of literature and truly constructive work that has been done on this subject, but to cast my lot with those who feel that the solution of a cure for recurrent dislocation of the shoulder will probably be found in the properly placed check ligament between the scapula and the humerus.

It is interesting to note that there has been a constantly increasing tendency of surgeons to resort to this type of procedure, Joseph, Rich, Gibson, Loeffler, Plummer, Potts, Wülfling and Hoke all reporting successful cases. The operations done by these men vary from the fixing of the head and tuberosity of the humerus to the acromion process by bands of fascia to fixing the anterior capsule to the acromion process by the same material. The principle of the latter procedure is to give a check ligament that will prevent the head of the humerus from sliding forward when the arm is in abduction and displaced slightly backward.

The operation we describe is essentially the same as that described by Plummer and Potts, having to our fancy two additional advantages. First, it shortens the relaxed capsule, and, second, we think it is a more simplified technic.

DESCRIPTION OF OPERATION

The shoulder joint is approached through the anterior incision extending from the acromion process downward, separating the fibers of the deltoid and exposing the anterior and inferior part of the capsule. The tendon of the long head of the biceps is identified and acts as a

guide to the line of fascial sutures. A strip of fascia is taken from the tensor fascia femoris and fixed to the Gallie type of needle, according to technic described by him. The arm is externally rotated to permit suturing as far forward as possible, and the fascia is laced into the capsule, as shown in figure 4. The capsule is then drawn taut, as shown in figure 5, and the lacing fixed firmly to the capsule by chromic catgut sutures. The fascia is then passed through the tip of the

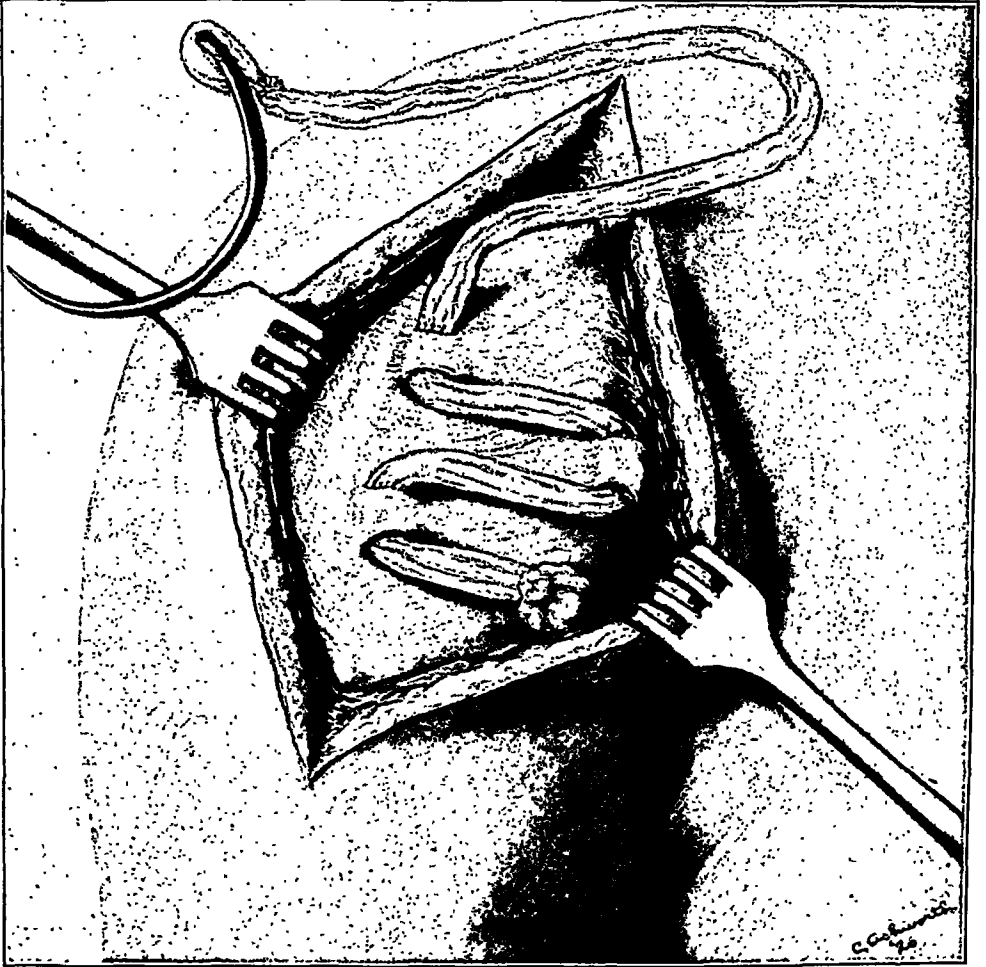


Fig. 4.—Fascia laced into relaxed capsule.

acromion process, either by a needle or by drilling a hole through the process, fixed at this point and again reattached to the anterior part of the capsule. Usually it is brought to a lower position than is shown in the accompanying illustration.

By this transplant and suture we have taken a slack from the anterior capsule and established a ligament extending from the acromion to the anterior capsule. The subscapular tendon may be included. We

believe that a ligament in this position reenforces the capsule in a way that prevents an anterior dislocation of the shoulder.

The arm is immobilized in a Velpeau type of bandage for a period of four weeks, after which gradual use is begun.

CASE 7.—W. O., a man, aged 20, approximately six months before examination dislocated his shoulder. He continued to play football during that season with the arm fixed to the side by an apparatus. In spite of this he had several

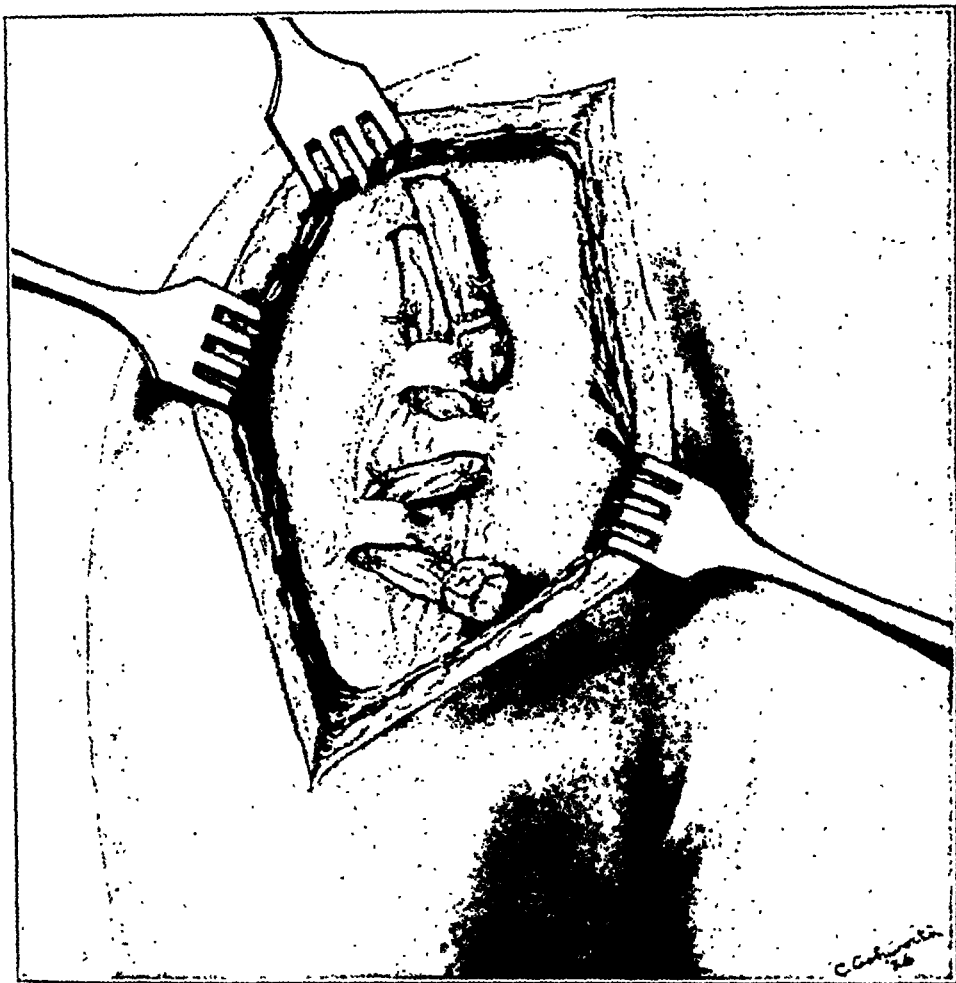


Fig. 5.—Relaxed capsule drawn taut and fixed; fascia inserted into acromion and reattached to capsule.

dislocations and was unable to indulge in any athletic sports that required the use of the arm. He presented a typical history and clinical picture of a recurrent anterior dislocation of the shoulder.

The operation described above was performed, Feb. 20, 1925, and the arm was immobilized in a Velpeau bandage for four weeks. Gradually exercise was taken. During the season of 1925 he played football on his college team without apparatus, having no difficulty with the shoulder. At present he states that he does not realize that he ever had any trouble with his shoulder.

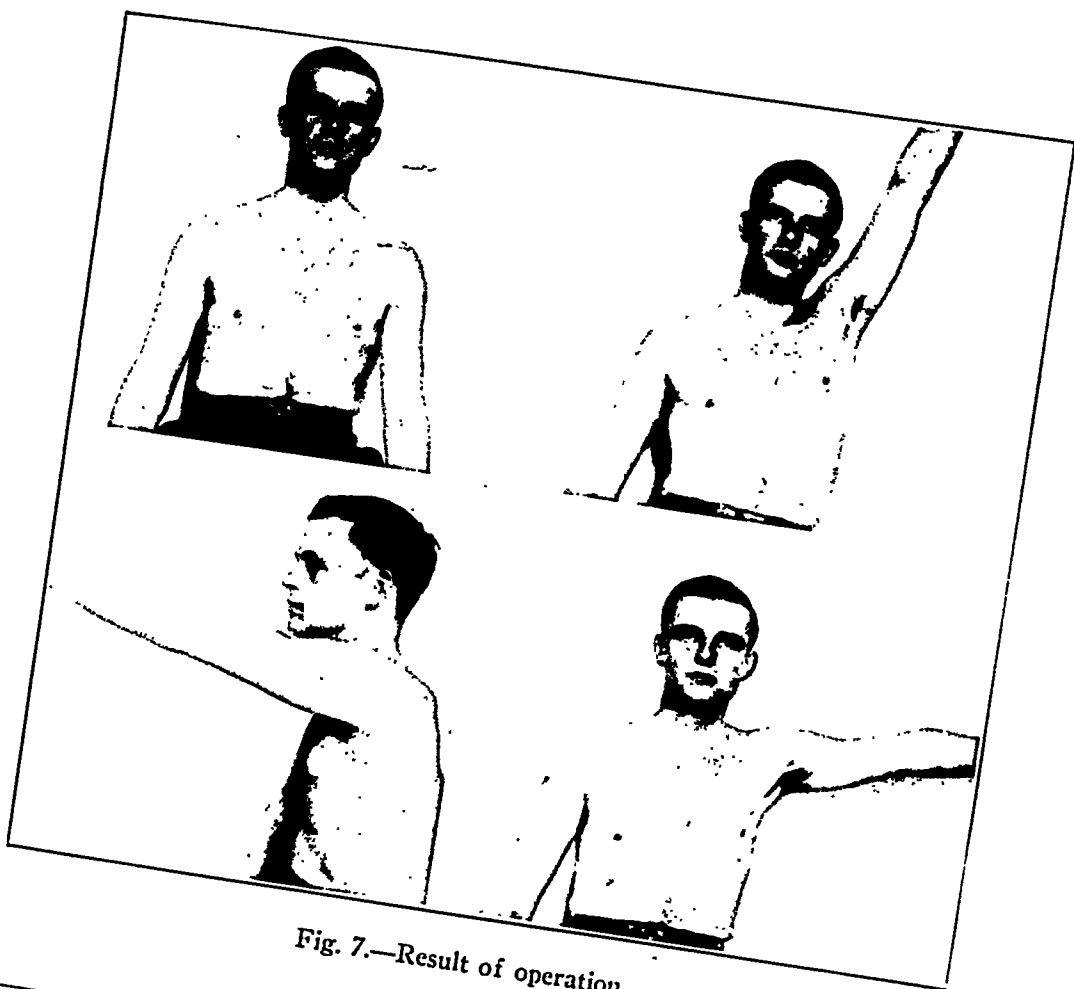


Fig. 7.—Result of operation.

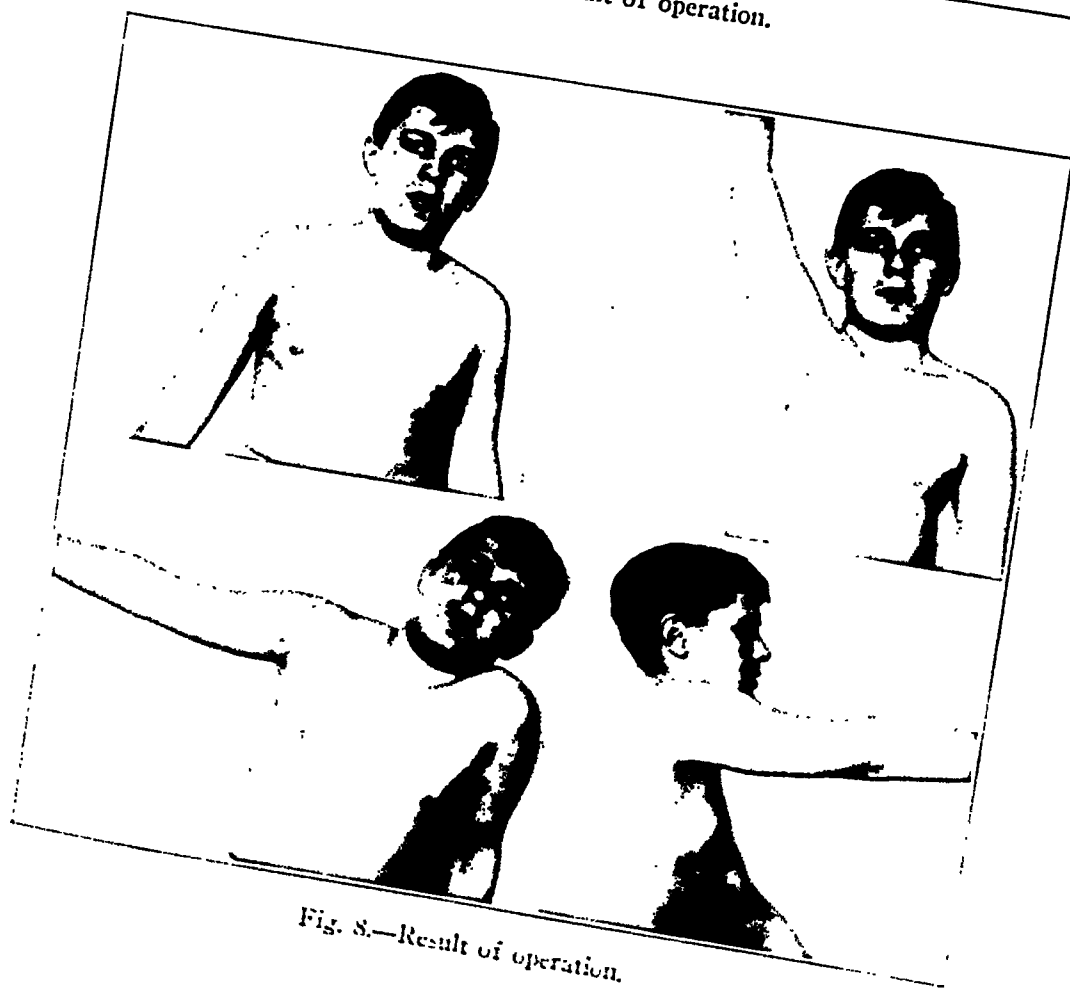


Fig. 8.—Result of operation.

lower level of the glenoid. An operation was performed, June 24, 1925. The horseshoe incision was made directly over the shoulder, the deltoid was retracted, the capsule was reinforced anteriorly, fascia being carried through the acromion; a similar procedure was applied to the posterior part of the capsule. The arm was immobilized in a Velpeau bandage for four weeks, followed by active exercise. April 2, 1926, the patient reported that he felt no discomfort in the shoulder, that he was engaging in active athletics, and could for the first time play baseball with boys of his age.

CASE 10.—M. W., a woman, aged 21, June 6, 1924, dislocated her right shoulder while pushing a piano. Since that time she had had six dislocations. She became so apprehensive that she scarcely used the arm at all. She was operated on Aug. 28, 1925, and reported April 2, 1926, that the arm gave her absolutely no concern.

UTILIZATION OF SKIN-MUSCLE PEDICLED FLAP IN OPERATION FOR LUNG ABSCESS

PRELIMINARY REPORT *

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SAYRE, PA.

In the descriptions that follow it will be easy to perceive the influence of Schede and Estlander, of Lockwood, Keller and Graham, for there is nothing new in large square or oval flaps when operating on the thoracic cavity, nor is there anything new in leaving skin edges unsutured after operations on infected areas. However, in the literature dealing with lung abscess, there have been discovered no references to the purposeful creation of a large skin-muscle pedicled flap, with the predetermined intent of suturing it to the chest wall, wide open, muscle side exposed, once the abscess cavity has been fairly opened, and so leaving it for four or five weeks, until secondary suture can be safely carried out. Such a procedure has given satisfactory results in a small series of cases, and therefore a preliminary report is now submitted.

Operation for lung abscess is far from being standardized. It is conceivable that never will it be fully standardized. There are many factors that make it a difficult subject to reduce to simple, definite statements. Even before electing a surgical policy the relative merits of postural drainage and of bronchoscopic treatment must be weighed. If surgery is decided on a host of variables is at once introduced. The anatomy of the anterior chest wall differs from that of the posterior chest wall. The approach to apex differs from the approach to base. The accessibility of the axilla is easy and the accessibility of the mediastinum is difficult. Fistulas are a source of trouble in one case and a safety device in another case. One abscess is at the periphery and another is deep within the substance of a lobe.

One of the greatest obstacles in the surgical care of lung abscess is inadequate access to the diseased tissue. The operative wound is, as a rule, too small to permit the complete mastery over the situation that must be exercised if the best results are to be attained. Furthermore, whatever is done under direct visual control is better done than that which is governed by blind touch. Throughout modern literature on lung abscess there is a decided trend in favor of greater accuracy of approach and more elaborate treatment of the lung tissue, even at the

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* Read before the New York Society for Thoracic Surgery, March 23, 1926.

expense of anatomic structures. The creation of a large opening in the chest wall helps to offset the difficulties that have just been mentioned.

Gradually, at the Robert Packer Hospital (Guthrie Clinic), a more and more radical operative policy has been employed in cases of lung abscess submitted to surgical treatment. Adequate access and constant

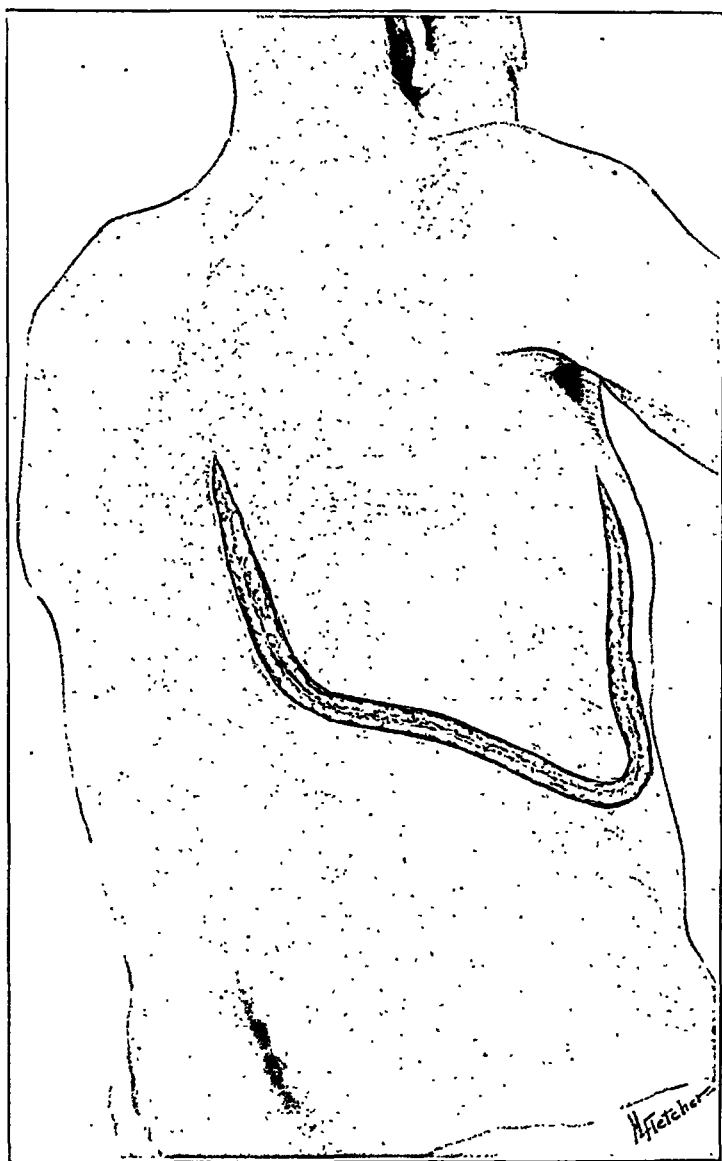


Fig. 1 (stage 1).—Preliminary incision showing relatively large size of flap; in this case the vascular hinge is at the superior border of the flap; it might equally well be placed at the posterior border.

visual control are the dominant concepts. The open flap and a radical attack on the chest wall are the tactical expressions of the determined strategy. Such an operation is best divided into stages. The history of the flap can be clearly traced through the several stages.

STAGES OF OPERATION

Stage 1.—The location and extent of diseased tissue is determined as accurately as possible by physical examination and roentgenograms. Aspiration is preferably omitted. It is a questionable procedure in cases of lung abscess. If pleural adhesions are present, little harm can be done. If adhesions are not present, there is serious risk of soiling the pleural cavity. The outlines of the flap are marked on the skin, roughly square, one side to remain as hinge and source of blood supply, the other three sides to be incised freely to the chest wall proper. Such

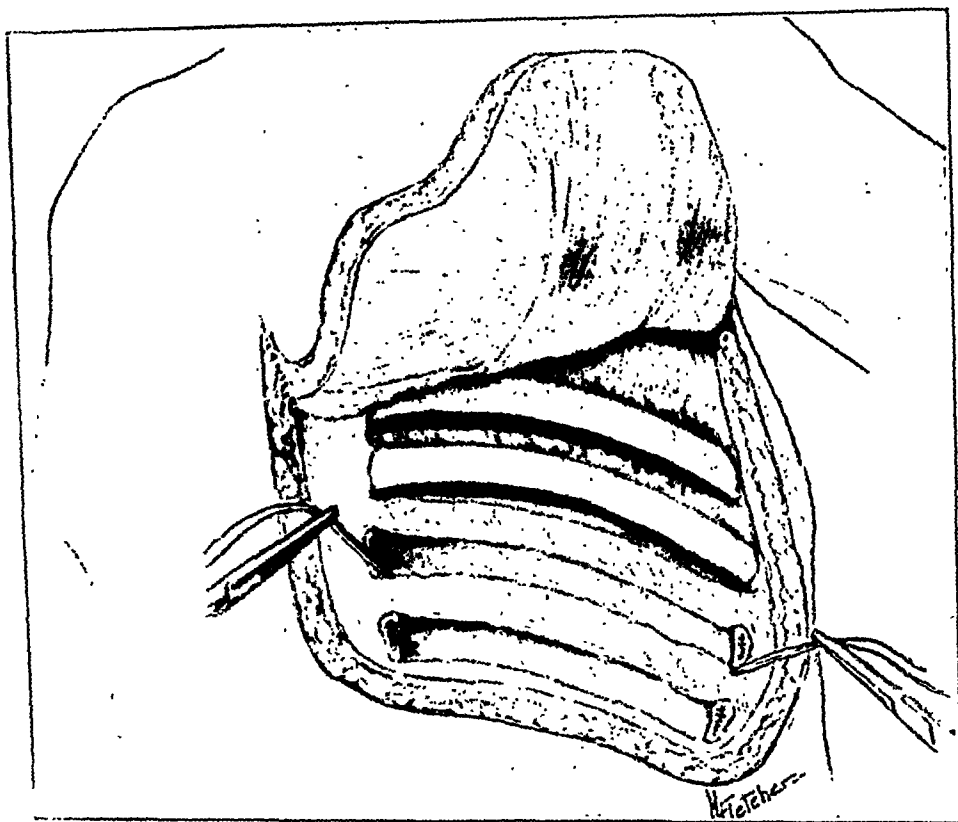


Fig. 2 (stage 1).—Flap turned up showing fibers of serratus and latissimus dorsi; ribs exposed and lower two resected.

a flap can best be utilized in the lower half of the chest; it is not so convenient for upper lobe approach, either anteriorly or posteriorly. The flap is laid wide open, immediately exposing the ribs and the intercostal structures. Subperiosteal resection of the exposed ribs, as many as may be necessary, is accomplished. The intercostal arteries, nerves and veins are ligated en masse at each rib stump. Through each periosteal sheath a small incision is made leading into the pleural cavity, and a finger tip is introduced to determine the presence or absence of adhesions. If no adhesions exist the lung is sutured to the

chest wall. Due care is exercised to prevent open pneumothorax—small exploratory incisions, gauze tampons, differential pressure. Ordinarily stage 1 ends at this point and the flap is replaced in its anatomic position and tacked down, muscle to muscle, skin to skin. Drainage may or may not be introduced beneath the flap. If adhesions

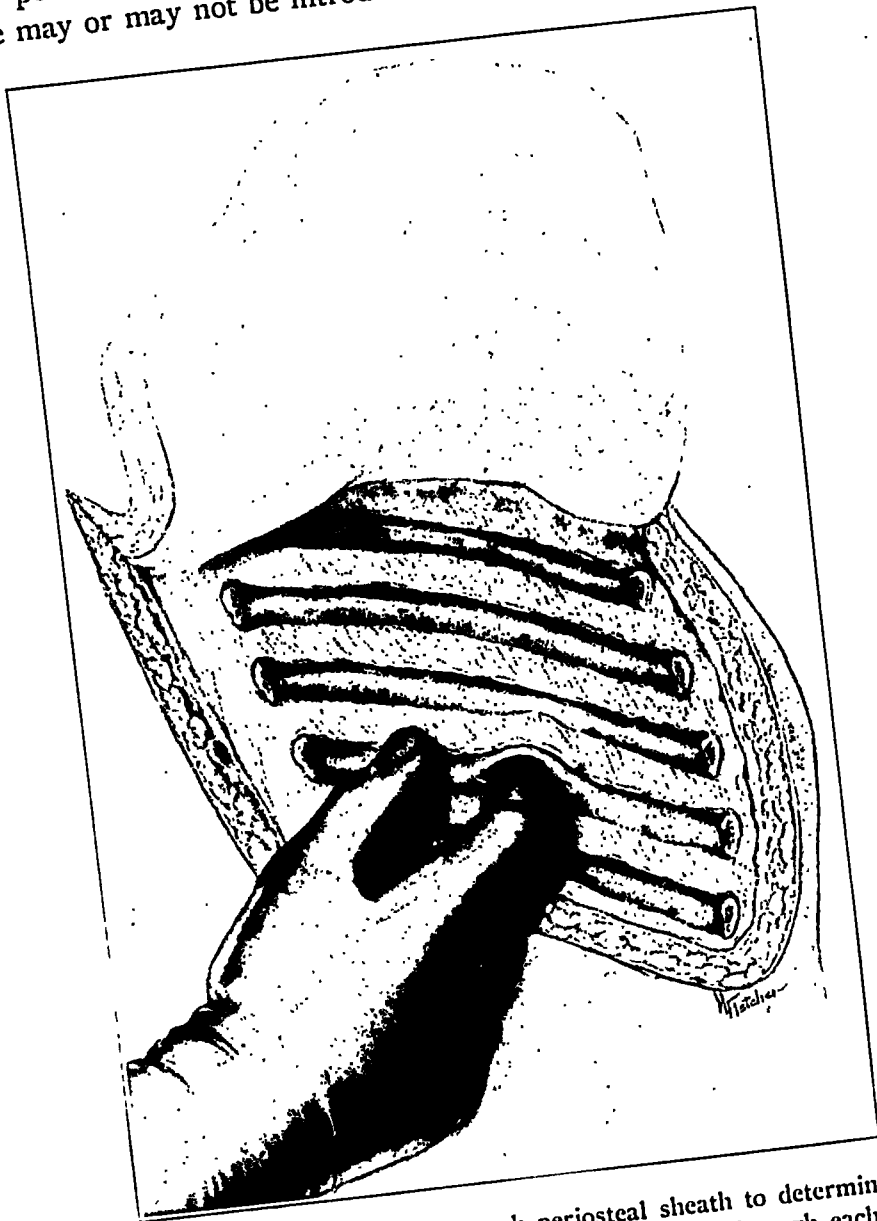


Fig. 3 (stage 1).—Exploration through periosteal sheath to determine presence or absence of adhesions; similar exploration is carried out through each periosteal sheath.

do not exist, and there is risk of pneumothorax, drainage has preferably been omitted.

The choice of the side to serve as the hinge may apparently be left to convenience. Actual experience has shown that the hinge may

be posterior, posterosuperior, superior or anterosuperior without adversely affecting the blood supply. There has been no experience with a flap involving the pectoral muscles or the region of the scapula.

Stage 2.—From three to five days elapse between stages 1 and 2. During this time the lymphatic spaces in the traumatized tissue have

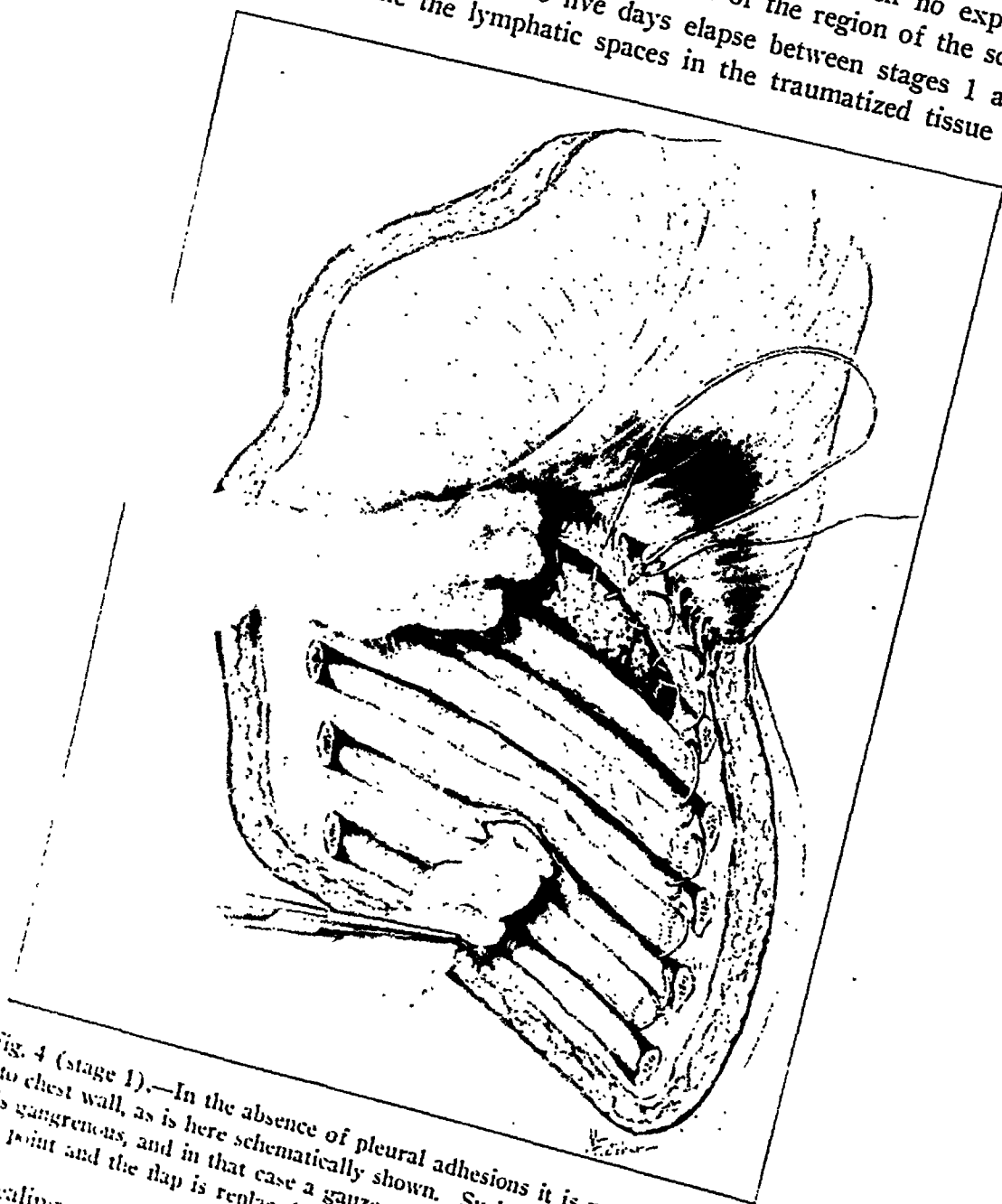


Fig. 4 (stage 1).—In the absence of pleural adhesions it is necessary to suture lung to chest wall, as is here schematically shown. Such suture is impossible if the lung is gangrenous, and in that case a gauze pack is utilized instead. Stage 1 ends at this point and the flap is replaced in its anatomic position.

been scaling off. The second stage is usually accomplished with little distress to the patient. The temporary tacking sutures are removed and the big flap is reopened. The intercostal muscles, periosteal sheaths

and other structures of the chest wall, together with the parietal pleura, are removed en masse, as in the Schede operation. The diseased lung is immediately beneath the eyes and hands of the surgeon. If adhesions are weak, or air is sucking around the edges of the chest wall defect, the flap may again be replaced for a period of one or two days before proceeding. Otherwise, the point of easiest access to the abscess cavity is determined by sight, palpation or needle, now fairly permissible for the first time, and an opening made boldly into the abscess

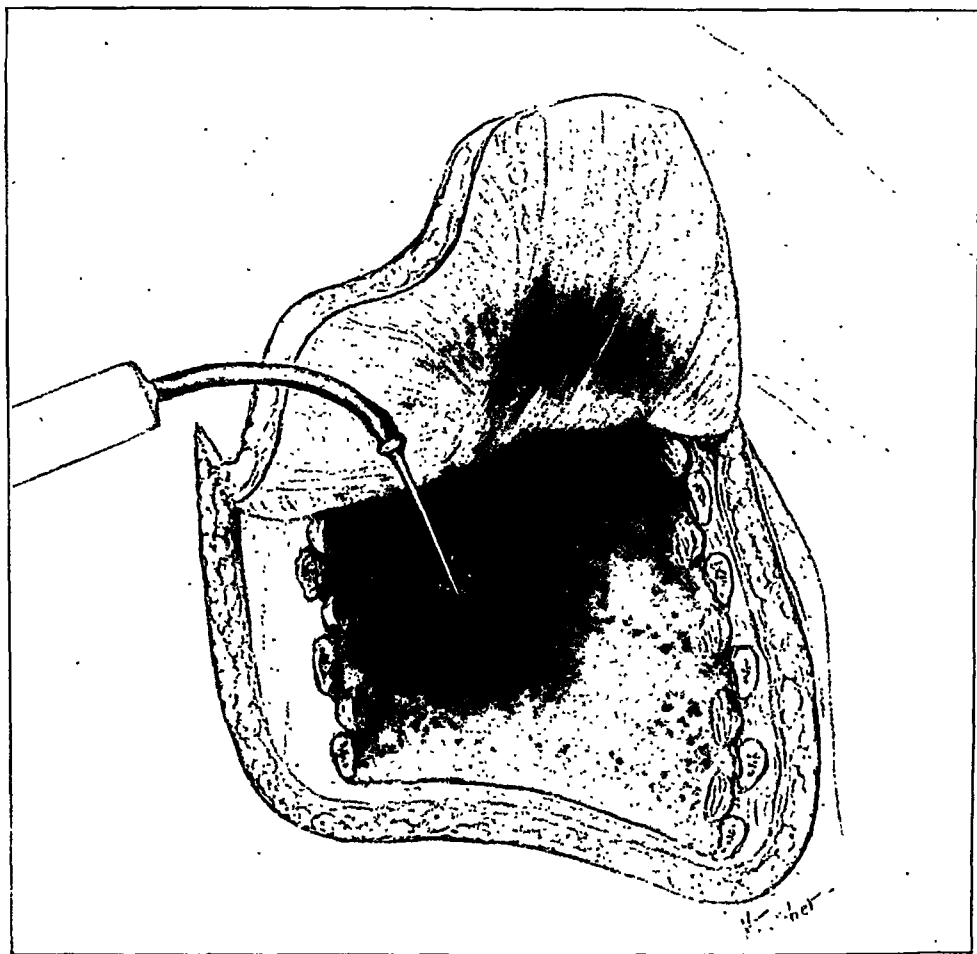


Fig. 5 (stage 2).—Flap reopened; soft structures and chest wall having been excised, the abscess area is located by sight, palpation or exploratory puncture.

cavity by blunt scissors, cautery, knife or trocar cannula. The opening is enlarged to a sufficient degree and packed wide open. The wound edges are protected with strips of petrolatum gauze. The flap is sutured wide open, muscle side exposed, and is so left until the lung tissue is clean enough to permit of secondary closure.

During the period of postoperative care and dressings the flap remains wide open. Constant access to the diseased lung tissue is

assured. The cautery may be employed; any suitable type of dressing may be utilized. Fistulas are under visual control. Accessory pockets can be reached with comparative ease. From time to time a suture holding the flap will pull out; it can be replaced as a minor operative procedure. The majority of patients require one or two elaborate dressings under gas during their period of after-care. It has required from twenty-four to thirty-nine days to prepare the wound for secondary closure. The average time has been thirty-three and one half

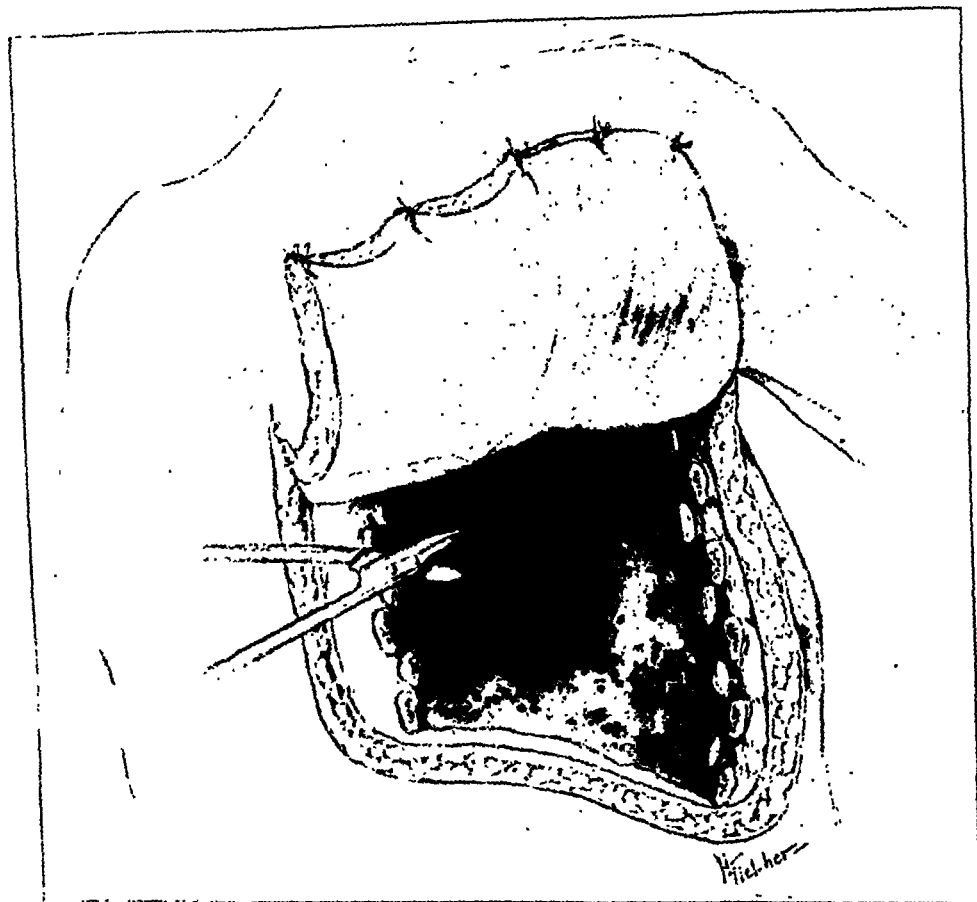


Fig. 6 (stage 2).—Abscess area widely opened by blunt scissors, fingers or cautery; flap is sutured to chest wall, muscle side exposed, and left in this position for from four to six weeks until secondary suture can be safely accomplished.

days. One patient, closed in twenty-four days, had to be reopened and secondarily treated. He then healed permanently.

Stage 3.—This is the simple anatomic replacement of the flap, muscle to muscle, skin edge to skin edge. It is, of course, necessary to freshen the skin edges, to release fibrous bands that tend to wrinkle the flap, and to isolate the edges of the sectioned muscles. A general anesthetic has been preferred for this stage. Safety requires that a

drain leading to the damaged lung tissue be left beneath the replaced flap. Within a relatively short time this may be discarded.

Actual experience with this operation at the Robert Packer Hospital has been limited to six cases. It was first used in January, 1925. The ages of the patients have varied from $2\frac{1}{2}$ years to 57 ($2\frac{1}{2}$, 40, 45, 48, 50 and 57). Four cases were diagnosed as abscess of the right lower



Fig. 7 (end-result).—Flap after secondary suture; the flap in this case had been open for thirty-five days.

lobe, and two of these had ruptured into the pleural cavity, giving rise to an empyema as well. One was diagnosed as gangrene of the right lower lobe. One was a subphrenic abscess. Two were postpneumonic. Three, including the subphrenic abscess, followed an

acute intra-abdominal disturbance (ruptured ulcer—ruptured appendix—empyema of the gallbladder). One abscess resulted from a pulmonary infarction seventy-eight hours after a Talma-Morrison operation for hepatic cirrhosis. In every instance, therefore, the thoracic condition was a complication or sequel to a severe illness. There was no mortality in the series.



Fig. 8 (end-result).—Flap after secondary suture; the flap in this case had been open for thirty-eight days; along the upper border of the picture can be seen points to which the flap had been sutured.

Twice stage 1 and stage 2 were combined and carried out as a single primary operation. In the other four instances the two stages were distinct and were separated by from three to five days.

During the after-care cauterization was utilized in two cases. The main reliance was placed, however, on careful dressing attention daily, or more frequently if necessary, and a firm belief that the increased aeration would assure the necessary tissue repair.

In one case the radical operation was done secondarily to a simpler, conservative drainage. The wound had not healed; a fistula had persisted; the patient was at a standstill. After the radical operation cure rapidly followed.

The procedure as described is confessedly radical. It may be criticized on that account; also because it demands a loss of anatomic structures, produces a permanent physiologic impairment, requires three or more operative steps, and presumably subjects the patient to a greater risk. There must be definite advantages to warrant its employment, and the net risk must not be prohibitive. The advantages may be summed up as:

1. Free, complete access to all diseased lung tissue, not only at the time of operation but throughout the entire period of after-care.
2. Free aeration of infected lung tissue.
3. Minimized risk of cellulitis of chest wall.
4. It is well tolerated by the patient and not painful.
5. Ultimate healing is more certain by virtue of the thoracoplasty which is really done at the time of the operation.

Time and further experience alone can determine the advantages and disadvantages of such a procedure and settle its merits. Only the future can evaluate the mortality risk, the subsequent incidence of chronicity, and the prospect of cure or benefit. This is merely a preliminary report. With the accumulation of additional data it is anticipated that a full critical study can soon be presented.

CERVICAL SYMPATHECTOMY

A REVIEW OF THE LITERATURE *

W. BLAIR MOSSER, M.D.

PHILADELPHIA

Surgical intervention with the cervical sympathetic nervous system is a much older procedure than is generally recognized. Prior to 1896 Thomas Jonnesco had performed an operation on the cervical sympathetics in forty-three cases of epilepsy and eight cases of exophthalmic goiter.¹ He gave very incomplete results, but in 1906 he again compiled and published a total of 159 cases in an article read before the German Surgical Congress,² many of which had been carefully studied and conscientiously followed. In this paper he reported twelve of 117 cases of idiopathic epilepsy absolutely cured, twenty-five cases of exophthalmic goiter completely recovered and two cases of tic douloureux, one of which was relieved for four years and the other for six months. The report of the two cases of tic was probably stimulated by Jaboulay's suggestion as early as 1899, when he also first suggested the procedure in exophthalmic goiter.

The case reports of epilepsy with recovery of the remarkable number of 10 per cent would seem to be one of the most noteworthy publications of the first part of the century and compares favorably with the 213 cases compiled by Winter³ a few years previously from several clinics, with 6.6 per cent of cures as compared to 0.79 per cent of cures by conservative treatment in a control series of 1,300 cases. Exception, however, has frequently been taken to the method of judging final results. As early as 1901, after a careful review of the whole matter, Brown⁴ declared the operation to be of no value and comparatively lately Brunning⁵ has again condemned the procedure.

In theory Jonnesco and Jaboulay agree that interruption of the continuity of the sympathetic system in the cervical region paralyzes vasoconstrictor influences, thus leading to a congestion of the motor cortex of the brain through passive dilatation of the cerebral vessels. This deduction was due, no doubt, to the very evident connection found

* From the Department of Surgery, University of Pennsylvania School of Medicine.

1. Jonnesco, Thomas: *Ann. Surg.*, 1897, p. 513.

2. Jonnesco, Thomas: *Tr. German S. Cong.*, 1906.

3. Winter, G. J.: *Arch. f. klin. Chir.* **67**:816, 1902.

4. Brown: *Arch. f. klin. Chir.* **64**:715, 1901.

5. Brunning, F.: *Med. Klin.* **19**:671 (May 30) 1923.

between the sympathetic ganglions and the internal carotid artery. They seem to disregard, however, that all investigations, anatomic and physiologic, tend to prove that the cerebral vessels, whether the brain is normal or abnormal, are entirely free of vasomotor influences. Their results, therefore, would seem to be unsound in principle, unsubstantiated by experimentation and dubious in actuality. Jonnesco himself appears to have recognized the fallacy of his theory, as he discarded the procedure soon after his report to the German Surgical Congress.

Jonnesco's report of marked improvement in exophthalmic goiter following bilateral cervical sympathectomy cannot be contradicted and has lately been shown to be based on a sound physiologic principle by Reinhard,⁶ who showed by photomicrographs that extirpation of the cervical sympathetics of a dog resulted in a reduction of the size of the thyroid on the side operated on, and that chronic irritation of the ganglions induced hypertrophy of the lobe on the side irritated. He therefore concludes that "exophthalmic goiter is entirely due to some abnormality of sympathetic innervation."⁶ Following his experimental work Reinhard has tried sympathectomy in eight cases with progressive decline of all symptoms until a complete cure occurred in each case. He excised the superior and middle ganglions with extirpation of the cervical trunk. He observed no ill effects.⁶ Deaver in 1902 reported several cases so treated with marked improvement but, following an unexplainable death in two of his series, he abandoned the procedure.

It is interesting to note that at about the time the controversy concerning the efficacy of sympathectomy in thyroid disease was at its height ligation of the arterial supply of the gland was first proposed and later became widely adopted, without, however, any apparent thought that the two procedures may have any connection until Crile only in recent years advocated this theory. It is now, I think, the universal opinion that the improvement from polar ligation is due to interruption of the sympathetic nerve supply and not to any interference with the mechanical distribution of the thyrotoxic products. This certainly appears to be the most logical explanation of the benefits of ligation, as it is inconceivable to suppose that a gland having the rich vascular anastomoses possessed by the thyroid could be materially influenced by merely ligating its large vessels, either in its nutrition, its metabolic activity, or by mechanically hindering the distribution of the comparatively minute amounts of thyroxin secreted daily. Since, then, the only communication between the cervical sympathetics and the thyroid is through the periarterial sympathetics, it would seem to be a much more logical procedure to interrupt this communication by an operation having practically no mortality than to subject the patient to one having an admittedly high

6. Reinhard, W.: *Deutsche Ztschr. f. Chir.* 180:170 (June) 1923.

one. However, it still remains for some one actually to prove that the benefits from ligation are due to sympathetic interruption by performing arterial decortication of the thyroid vessels, with careful subsequent observation.

We cannot, of course, disregard the cases of Reinhard, Jaboulay and Jonnesco in which absolute cure was asserted, especially since the most ardent advocate of ligation can claim a cure in only a very small percentage of cases, this operation being used only as a preparation for thyroidectomy. Since, then, a certain percentage of cures can be attained by avulsion of the cervical ganglions the question naturally arises as to whether this operation should supplant thyroidectomy. Klose and Hellwig⁷ of Berlin have recently reviewed the whole matter with the careful clinical study of many cases and have come to the conclusion that cervical sympathectomy for exophthalmos may be of some value in severe cases but does not compare with thyroidectomy. This seems to be the general opinion of the great majority of surgeons who are doing "goiter work."

From 1905 to 1915 there was a distinct decline of interest in sympathectomy but in 1916 interest was again revived when Jonnesco first tried the operation as a treatment for angina pectoris. The inspiration cannot be attributed to Jonnesco, however, for as early as 1899 François Franck first suggested severance of the sympathetic nervous supply of the heart as a rational procedure in angina.⁸ Neither he nor anyone else, however, attempted the operation until seventeen years later when Jonnesco selected a well marked and typical case and put the thought into execution. This case, with reference to four others, was reported in 1920.⁹ His patient was a man of 38, having typical anginal pains at frequent intervals. He was free of a syphilitic history. The operation consisted of ablation of the middle and inferior cervical ganglions and of the first thoracic ganglion, together with avulsion of the cervicothoracic cord between these levels. The operation was confined to the left side. The patient showed no ill effects, convalesced rapidly and was immediately relieved of all symptoms. This relief had been permanent over a four year period when the case was reported. One year later Jonnesco reported the same case at which time he pronounced it as a cure,¹⁰ and a few months subsequent to this he reported in detail progressive improvement, but not absolute cure of his second patient, a man of 54 with typical anginal pains, six months following the same operation.¹¹

7 Klose, H., and Hellwig, A.: *Klin. Wchnschr.* 2:627 (April 2) 1923.

8 Franck, François: *Bull. Acad. de méd., Paris*, May 30, 1899, p. 594.

9 Jonnesco, Thomas: *Bull. Acad. de méd., Paris* 84:93 (Oct. 5) 1920.

10 Jonnesco, Thomas: *Presse méd.* 29:193 (March 9) 1921.

11 Jonnesco, Thomas: *Bull. Acad. de méd., Paris* 86:208 (Oct. 25) 1921.

The immediate results of these articles was to stimulate a renewed interest in the physiology, distribution and pathologic physiology of the cervical sympathetics. These investigations, however, were self-limited; first, because of the impossibility of producing the disease in animals and, second, because of the different anatomic arrangement and distribution of the sympathetics as found in the lower animals. Meltzer in 1920 excised the entire cervical gangliated chain in twenty-eight rabbits and eighty-three cats. Of these, twenty-five rabbits died within ten days and two cats within three days. With the exception of four all of the animals subsequently died, and of the four surviving ones two gave a negative paradoxical eye reflex, showing that the ganglions were not completely removed. Montgomery,¹² on the other hand, at about the same time reported that practically all his animals (cats, rabbits and rats) survived total ablation without any untoward symptoms. He concluded that complete ablation can only be asserted after histologic examination and not by physiologic methods. He also concluded that the sympathetic chain has in itself no endocrine function. Jonnesco, too, refutes Meltzer's analogy by stating that in more than 200 patients operated on between 1896 and 1923 he had never observed such disasters in human beings, either during or after the operation, as were observed in animals.

Following Jonnesco's two cases Tuffier reported a third case following the same technic, with marked improvement.¹³ Both these men insisted that only by severance of the cord below the superior ganglion could the impulse be interrupted. Bruning,¹⁴ however, disagreed with this view and, disregarding the fact that the superior ganglion has apparently no connection with the brain, he advocated its removal. His case, which was the fourth reported, was treated by complete ablation of the three cervical ganglions and the first thoracic. He reported complete relief of symptoms with lowering of the blood pressure.

Following these reports the literature has been abundant with case reports of complete or partial relief by performing Jonnesco's original operation. Borchard¹⁵ reported operation in a man of 54 with complete relief until death three weeks later. In our own country Reid and Friedlander¹⁶ of Cincinnati have carefully observed their first two reported cases with symptomatic relief in both, and Smith and McClure¹⁷

12. Montgomery, M. L.: *Endocrinology* 7:74 (Jan.) 1923.

13. Tuffier, T.: *Bull. Acad. de méd., Paris* 86:99 (July 26) 1921.

14. Bruning, F.: *Klin. Wchnschr.* 2:777 (April 23) 1923.

15. Borchard, A.: *Arch. f. klin. Chir.* 127:212, 1923.

16. Reid, M. R., and Friedlander, A.: *Sympathectomy for Angina Pectoris*, *J. A. M. A.* 83:113 (July 12) 1924.

17. Smith, F. J., and McClure, R. D.: *Surg. Gynec. Obst.* 39:210 (Aug.) 1924.

have recently reported two cases improved. Diez¹⁸ has reported three patients cured.

Kappis,¹⁹ by the technic of Bruning (total ablation), has operated on a considerable number of patients with good results in all, except one patient in which recurrence of all symptoms occurred four months after operation.

Pleth²⁰ reported four cases operated on by the Jonnesco method with one death due to postoperative pneumonia. The other three patients are living and have no symptoms.

Hofer and Eppinger,²¹ believing that the sensory impulse was carried only by the depressor nerve of the heart, which has its distribution to the suprasigmoid portion of the aorta, early took exception to the Jonnesco operation and advocated section only of this nerve. The depressor nerve was first described as early as 1866 by Ludwig and Cyon in their studies on the rabbit. It arises typically from two heads, one from the superior laryngeal and the other from the vagus, then either reenters the vagus to reach the aorta or courses down along the prevertebral fascia as an independent nerve. Often, however, it is entirely absent, in which case its function is apparently taken up by the vagus.

In their assumption, Hofer and Eppinger have been substantiated by the researches of Tschermak,²² who found that the depressor nerve is distributed entirely to the proximal aorta, has many connections with the cervical sympathetics, terminates in the jugular ganglion of the vagus and is entirely sensory in function. Tschermak also found that in health stimulation produced a general vasodilatation but when the arch is diseased vasoconstriction results.

Hofer's²³ first patient was operated on in 1922. The patient had typical anginoid pain on both sides of the body. A bilateral operation was performed. The patient recovered and was permanently relieved for two years, when she died of an intercurrent infection. Thus encouraged, Hofer and Eppinger continued their work and in 1923 reported six cases, with four completely recovered, one doubtful and one death from pneumonia.²¹ During the current year they again compiled their cases and reported fourteen, in which two of the patients died. In one a bilateral operation was performed in two stages. The depressor on the left was severed. On the right no depressor was

18. Diez, J.: *Rev. Asoc. méd. argent.* **37**:5 (June) 1924.

19. Kappis: *Med. Klin.*, Nov. 18, 1923.

20. Pleth, V.: *Am. J. Surg.* **36**:300 (Dec.) 1922.

21. Hofer and Eppinger: In *offizielles Protokoll der Gesellschaft der Aerzte*
11. Wien. *Wien. klin. Wchnschr.* **36**:534, 1923.

22. Tschermak, A.: *Wien. med. Wchnschr.*, 1924.

23. Hofer: *Wien. med. Wchnschr.*, May, 1924.

found, so the vagus was sectioned below the inferior laryngeal. Pain disappeared but the patient died suddenly two weeks later of no obvious cause. The second mortality occurred in a patient in whom no depressor nerve was found, in consequence of which extirpation of the cervical sympathetics was performed. He died five hours later from pulmonary edema.²³

They report that in all cases in which the depressor nerve was found and cut pain was immediately and permanently relieved and conclude, therefore, that section of this nerve alone will accomplish the same result as ablation of the cervical ganglions, that it is a more logical procedure, is substantiated by experimental findings and offers the least number of technical difficulties. They further suggest that Jonnesco may have sectioned the depressor nerve thinking that it was the superior cardiac nerve in his operation.²¹

The latter statement Jonnesco not only forcibly denies but also asserts that it is utterly impossible completely to interrupt the afferent pathway without ablation below the superior cervical ganglion.²⁴ He further objects to the procedure, not only because of the difficulty of isolation of the depressor nerve, due to individual variation and inconstancy of origin from the vagus, but also because of the danger of injuring the superior laryngeal nerve, which seems to have occurred in one of Hofer's series, necessitating tracheotomy and ending in death. At any rate it would be just as plausible to assume that Hofer had sectioned the superior cardiac nerve, thinking it was the depressor, as to assume that Jonnesco was in error.

There were now before the profession two different operations, both apparently benefiting the same condition. To these Coffey and Brown²⁵ in November, 1921, added a marked variation, which later became so modified that it may well be considered as a third form of operation. After selecting a patient with typical angina they decided to do the operation in two stages, the first stage being confined to section of the cord below the superior ganglion and section of the superior cardiac nerve. Following this part of the operation, on the left side only, the patient was completely relieved of pain. They, therefore, decided to do nothing further, and the patient remained entirely free of pain for one year when he was lost track of. They then selected four more cases and performed the same operation on them; that is, section only of the gangliated cord and the superior cardiac nerve close to the ganglion. This made a total of five cases that were reported in 1923,²³ with complete relief in two, partial

24. Jonnesco, Thomas: *Presse méd.* **32**:138 (Feb. 13) 1924.

25. Coffey, W. B., and Brown, P. K.: *Surgical Treatment of Angina Pectoris*, *Arch. Int. Med.* **31**:200 (Feb.) 1923.

(almost complete) relief in two and one death six hours after operation due to "acute vasomotor disturbance with dilatation of the heart."

One of these patients subsequently had a return of most of his symptoms, which would appear to be a fortunate occurrence, as it stimulated in these workers a most happy inspiration. They decided to avulse the superior ganglion.²⁸ This was done and the patient was completely and permanently relieved of all symptoms.

Following recovery of this patient Coffey and Brown decided to change their operative procedure and to avulse the superior ganglion after sectioning the superior cardiac nerve. This they did in eight cases which were thoroughly studied both before and after operation. Of these eight patients one died as the result of operation, and one two weeks later of myocardial disease. Five were completely relieved and the sixth was relieved of all pain except that referred to the left arm. They concluded that their results were due to severance of the superior cardiac nerve, which they considered as a vasoconstrictor one and not sensory, thus removing spasm of the aortic arch and of the coronary vessels.

There are now, therefore, the following operations before the profession, each with its advocates and each apparently successful in the treatment of the same condition:

1. Jonnesco's original technic: extirpation of the middle and inferior cervical ganglions and the first thoracic ganglion, with or without severance of the superior cardiac nerve.

2. Bruning operation: extirpation of the three cervical and the first thoracic ganglions.

3. Resection of the superior cervical ganglion and severance of the superior cardiac nerve as advocated by Coffey and Brown.

4. Severing the depressor nerve as practiced by Hofer and Eppinger.

In attempting to determine which of these various operations is correct in theory, it becomes necessary to inquire into the pathologic physiology of angina. Of the many theories advanced the following appear to have the most support:

1. That angina is due to myocardial exhaustion.

2. That angina is due either to coronary artery disease or to coronary spasm.

3. That it is due to an arteritis of the first part of the aorta.

The first theory has as its warmest advocate Danićopolu who contends that angina is due to "cardiac fatigue" caused by intoxication of

28. Coffey, W. B., and Brown, P. K.: Surgical Treatment of Angina Pectoris, *Arch. Int. Med.*, **34**:417 (Oct.) 1924.

the myocardium by incompletely eliminated fatigue products. In this he was supported by the late Sir James Mackenzie, whose only difference of opinion was an academic one.

The second theory is the oldest and for many years the didactically accepted one until Sir Clifford Allbutt made his extensive studies of angina and concluded that the symptoms are always due to disease of the suprasigmoid region of the aorta. He has "failed to discover an example of unmistakable angina in which, whatever the disease of the coronary arteries, the aorta, on careful examination, was shown histologically to be inwardly and outwardly sound."²⁷ This opinion has lately also been shared by Vaquez and Wenckebach. Wenckebach admits the presence of coronary disease in many instances but contends that all such cases have associated disease of the proximal aorta and, in addition, that in many cases of true angina only the latter pathologic condition can be demonstrated. He thinks that the cardiac failure is the result and not the cause of angina.²⁸

The latter hypothesis being accepted as the correct one, the cause of sudden death during the attack has led to much controversy and difference of opinion. Most of the observers agree that there is a sensory stimulus originating in the suprasigmoid portion of the aorta which is transmitted to the cardio-aortic plexus and carried from there, chiefly by the superior cardiac nerve, but in some instances also by the middle and inferior cardiac nerves to the cervical sympathetic ganglions. The exact course of the impulse from this point is somewhat confused, some physiologists contending that the impulse on reaching the superior cervical ganglion is immediately transmitted to the vagus through the small branches connecting the superior ganglion with the ganglions jugulare and nodosum, while others contend that the impulse first travels down the sympathetic chain to at least the first and probably second and third thoracic ganglions before its transmission to the central nervous system.

Acceptance of the latter as the most probable path is largely due to the work of Mackenzie²⁹ and Head³⁰ on the distribution of referred cardiac pain. The studies of these men have clearly shown that the cutaneous areas to which the pain is referred are supplied by the same spinal segments that receive the afferent impulse. Thus, we find that the pain of angina is usually referred to the anterior chest wall and to the inner side of the arm. The chest area is supplied chiefly through

27. Allbutt: *Diseases of the Arteries, Including Angina*.

28. Wenckebach, K. F.: Paper read before the Royal College of Surgeons, *Brit. M. J.* 1:826 (May 10) 1924.

29. Mackenzie, J.: *Diseases of the Heart: Symptoms and Their Interpretation*, ed. 3, 1918.

30. Head, H.: *Brain* 16:2, 1893; *ibid.* 17:339, 1894.

the second, third and fourth thoracic nerves. The intercostobrachial nerve, which originates from the second and third thoracic nerves, supplies the skin of the upper and inner side of the axilla and arm. It is through the connection of the intercostobrachial and the greater and lesser internal cutaneous nerves that the pain reflex radiates down the inner side of the arm.

Mackenzie's²⁹ conception of the production of the reflex is probably the most logical of the various ones advanced. He thinks the afferent impulse after descending the sympathetic chain enters the spinal cord through the white rami of the first, second and third thoracic segments. Normally, this impulse is imperceptible and is constant and uniform. Abnormally, however, the impulse from the diseased arch produces a hyperirritability of these segments and consequently the efferent impulse, which the body has learned to refer only to the somatic distribution of the segments, is also hyperirritable and produces the sensation of pain.

Whether the reflex has its synapse in the cord or in the brain is problematical. That it does reach the brain is generally accepted, largely on account of the observations of Byrne and Einthoven³¹ on "action curves" as recorded by the electrosympathicogram; that the impulse ascends through the vagus, however, is questionable, for if this were true the synapse should occur with the nuclei of the glossopharyngeal, the spinal accessory and the trigeminal, and the pain should be distributed in these nerves, which, as is well known, is never the case.

Acceptance of these hypotheses, to which at present there is little dissension, means also acceptance of the theory of retrograde transmission of the impulse through the sympathetic chain, rather than its immediate conveyance from the superior sympathetic ganglion to the vagus.

The immediate cause of death is thought to be vagus inhibition, which occurs with each attack and is supposed to vary in proportion to the intensity of the afferent stimulus.²⁷

As regards the depressor nerve there is no doubt of its existence and specificity in cats and rabbits. It is entirely afferent. If the central end of the cut nerve is stimulated, a marked fall of blood pressure with slowing of the heart results.³² Einthoven has shown by action curves that each heart beat sends an impulse over it.³³ As previously mentioned the anatomy of this nerve was first described by Ludwig and Cyon in 1866, who found that it originates by two heads, one from the vagus and the other from the superior laryngeal, then either courses down along the prevertebral fascia or reenters the vagus. It is dis-

31 Byrne, J. and Einthoven, W.: *Am. J. Physiol.* 65:350 (July) 1923.

32 Fyster and Hocker: *Am. J. Physiol.* 21:373, 1908.

33 Einthoven: *Quart. J. Exper. Physiol.* 1:243, 1908.

tributed to the proximal aorta. In man, however, the nerve is very inconstant in appearance and in many instances is entirely absent, in which case its function is taken up by the vagus. It is this nerve which Hofer and Eppinger have sectioned and concerning which they have had so much controversy with Jonnesco.³⁴

The question now arises as to whether the interrupted impulse is afferent or efferent. Pleth has considered it to be the latter and thinks his results are due to abolition of the abnormal vasoconstrictor impulses destined for the root of the aorta; the pain being due to anemia of this region. Coffey and Brown are of the same opinion. Practically all others think it is the sensory pathway that is interrupted, and in this they are supported by physiologic experimentation. In the light of our present knowledge, it would seem that afferent interruption is the most logical theory.

It will now be seen that there are apparently two afferent pathways from the aorta, first, through the superior cardiac nerve to the cervical sympathetics and, second, through the depressor nerve directly to the vagus; furthermore, that interruption of either pathway produces the same results. On closer scrutiny, however, this may not be the case. There seems to be an utter disregard of the fact that there are many communications between the depressor nerve and the cervical sympathetics on one hand²² and at least two constant connections between the superior cervical ganglion and the vagus. Does it not seem logical to assume that the afferent pathway, regardless of whether it is carried by the superior cardiac nerve or the depressor nerve, must always pass through the cervical sympathetics before its transmission to the central nervous system? This would explain the similar results obtained by Hofer and Jonnesco by what, at first glance, appear to be totally dissimilar procedures. They have interrupted the pathway of sensory impulse regardless of whether that interruption is produced in the sympathetic chain or in the depressor fibers.

The apparent dissimilarities between the various procedures carried out on the cervicothoracic cord are interpreted much more easily. It is merely a question of interrupting the impulse at different levels. The fact that interruption by ablating the cord below the superior ganglion produces the same result as severance of the superior cardiac and ablation only of the superior ganglion lends credence to the theory that all afferent impulses have a retrograde transmission through the cervical chain before reaching the central nervous system. It is entirely probable that all afferent impulses must enter the chain through the superior cardiac nerve, first, because it is this nerve that is distributed to the proximal aorta and, second, because the communication between the

34. Jonnesco (footnotes 21 and 24).

sympathetics and the depressor nerve is through the superior cardiac. This it appears would adequately explain the uniformity of results obtained by Jonnesco, Bruning and Coffey by operating at different levels.

If we admit, then, that these three types of operation are the same in principle, the question naturally arises as to which should be the operation of choice. In deciding this the technical difficulties alone should be the deciding factor. Because of the inconstancy in origin, frequent absence and difficulty of recognition, section of the depressor nerve would appear to offer the greatest technical difficulties and, therefore, should be avoided.

Of the various procedures on the cervical sympathetics themselves the minimum surgical intervention which will produce the maximum result should be selected. In determining the extent of operation one must bear in mind many points. Jonnesco has consistently asserted that avulsion of the middle and inferior ganglion with the first thoracic is not only absolutely necessary to obtain results but also is a safe procedure,³⁵ while Daniëlopolu, on the other hand, is uncompromisingly opposed to removal lower than the middle ganglion, as he believes that three of Jonnesco's patients died from avulsion of the inferior ganglion.³⁶ Certain it is that avulsion of only the superior ganglion, with severance of the superior cardiac nerve, offers the least technical difficulties and, since the results from this operation compare favorably with the results of more extensive procedures, this would appear to be the operation of choice. The question now arises as to whether a unilateral or bilateral operation should be performed. If the pain is entirely left sided the operation should first be performed on that side with subsequent, but later, operation on the opposite side if symptoms persist or return. In cases of bilateral reference of pain a bilateral operation should be performed, but in stages, the second stage to succeed the first by an interval of not less than from seven to ten days.

The operative technic to those having a thorough knowledge of the surgical anatomy of the neck is simple. It is not, however, a procedure to be recommended to the inexperienced. A longitudinal incision is made along the border of the sternocleidomastoid muscle, exposing it; this muscle is then either retracted backward or split with its fibers through the posterior half. This exposes the sheath containing the vein, artery and vagus nerve. These are retracted toward the midline with two hand retractors, sufficiently separated to expose the prevertebral space through a considerable length. The prevertebral fascia is now denuded and shining through it will generally be seen the sympa-

³⁵ Jonnesco, Thomas. *Presse méd.*, May 23, 1923.

³⁶ Daniëlopolu, D. *Brit. M. J.* 2:553 (Sept. 27) 1924.

thetic chain. If not, the fascia is carefully incised and stripped back, thus bringing the chain into the field of operation. The nerve is picked up and is then readily followed upward to the superior ganglion where the superior cardiac nerve can be isolated without difficulty and severed. The superior ganglion is then ablated. If further ablation is decided on, the procedure is carried out from above downward, bearing in mind the more common anomalies of the sympathetic chain. The middle ganglion is frequently absent, or the third cervical one may be fused with the first thoracic ganglion. It should also be remembered that exposure of the first thoracic ganglion is rather difficult.

In attempting to estimate the results of sympathectomy for angina there is considerable difficulty. A disease concerning which so little is really known of its pathology and physiologic pathology, whose progress is so variable, whose prognosis is so guarded, whose termination may be sudden death at any stage of an apparently mild case, and in which our present instruments of precision give us so meager knowledge, scarcely lends itself to satisfactory observation after any form of treatment. That sympathectomy does in a great many instances temporarily, and in the majority of cases permanently, relieve the patient of practically all his pain cannot be denied. That it does anything further is only a matter of conjecture. Its most ardent supporters measure success only by relief of pain, and Daniélopou³⁰ and Wenchebach²⁸ have repeatedly emphasized that there is no other benefit. But is this a benefit? Is pain not the distress signal that warns the patient to relax completely and rest until the heart has recovered? Do these patients who are relieved of this "danger signal" exterminate themselves by an unconscious disregard of nature's warning? Who can say? It is true that many of the patients operated on have died suddenly and of no apparent cause, but by what means can we judge that such a catastrophe would not have occurred if the course of their disease were not interfered with? Is not relief of the physical pain and horrible mental anguish sufficient justification for the operation? These are questions just as incapable of solution at the present time as is the nature of the disease itself. We must wait for further knowledge and further observation before attempting to solve them.

EXTRACRANIAL ANEURYSM OF THE INTERNAL CAROTID ARTERY

HISTORY AND ANALYSIS OF THE CASES REGISTERED UP
TO AUG. 1, 1925 *

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While extracranial aneurysm of the internal carotid artery is not a common condition, it is by no means as infrequent a lesion as hitherto supposed. In a paper in 1921, I was able to compile out of the literature sixty-nine cases, to which I added a personal observation.¹ At that time I thought I had exhausted the field, only to discover later, in a source unavailable then, a number of additional examples of this lesion. By adding these and some cases that have appeared in the more recent literature to my earlier compilation, the recorded instances of extracranial aneurysm of the internal carotid artery show the no insignificant total of 106 cases, divided as follows: spontaneous, forty-two; erosive, eighteen; traumatic, twenty-six; arteriovenous, nineteen, and unclassified, one.² But it is not so much the rarity of this lesion, when it does occur, that commands our attention as its propensity to imitate peritonsillar abscess, which habit of mimicry has led on more than one occasion to its lancing, with a mortal hemorrhage. The majority of these patients should recover if the aneurysm is promptly recognized and properly treated, but an overwhelming proportion die under dilatory, blundering or pernicious tactics, as the accompanying tables bear testimony; for this reason I have thought the completion of the history of this lesion of some value to the profession.

Of the 106 patients, forty-nine recovered; two showed improvement; seven were unimproved; the condition of one was not stated and forty-seven died (Table 1). Seventy were operated on, with forty-six cures, two improvements, one recurrence and twenty-one deaths (Table 2). Thirty-five were not operated on, with three cures, six unimproved, one the condition not mentioned and twenty-five deaths (Table 3). One case was found in a dissecting room subject, with no available history,² so is valueless for statistical purposes.

Fifty-nine of these patients were operated on since 1880, with forty-one, or 69.49 per cent., cures; two, or 3.39 per cent., improvements;

* From the surgical department of the University of Maryland School of Medicine and College of Physicians and Surgeons.

1. Winslow, Nathan: *Tr. South S. A.* 34:323, 1921; *Ann. Surg.* 75:694, 1922.

2. Arnould: *Bull. et. mém. Soc. anat. de Paris* 89:168, 1914.

one, or 1.69 per cent., recurrence, and 15, or 25.43 per cent., deaths. Forty-four patients were operated on since 1900, with thirty-one, or 70.45 per cent., recoveries; two, or 4.55 per cent., improvements; one, or 2.27 per cent., recurrence, and ten, or 22.73 per cent., deaths. On the other hand, of the thirty patients not operated on since 1880,

TABLE 1.—*Summary of Cases*

| | Cured | Improved | Unimproved | Uncertain | Died | Total Cases |
|--------------------|------------------|-----------------|-----------------|----------------|------------------|-------------|
| Spontaneous..... | 18, or 42.86% | 0 | 5, or 11.90% | 1, or 2.38% | 18, or 42.86% | 42 |
| Erosive..... | 6, or 33.33% | 0 | 0 | 0 | 12, or 66.67% | 18 |
| Traumatic..... | 12, or 46.15% | 0 | 1, or 3.85% | 0 | 13, or 50.00% | 26 |
| Arteriovenous..... | 13, or 68.42% | 2, or 10.53% | 1, or 5.26% | 0 | 3, or 15.79% | 19 |
| Unclassified..... | 0 | 0 | 0 | 0 | 1, or 100.00% | 1 |
| Total cases..... | 49, or 46.23% | 2, or 1.89% | 7, or 6.60% | 1, or 0.94% | 47, or 44.34% | 106 |

TABLE 2.—*Patients Operated On*

| | Cured | Improved | Unimproved | Died | Total Cases |
|--------------------|------------------|-----------------|----------------|------------------|-------------|
| Spontaneous..... | 16, or 64.00% | 0 | 0 | 9, or 36.00% | 25 |
| Erosive..... | 5, or 55.56% | 0 | 0 | 4, or 44.44% | 9 |
| Traumatic..... | 12, or 60.00% | 0 | 0 | 8, or 40.00% | 20 |
| Arteriovenous..... | 13, or 81.25% | 2, or 12.50% | 1, or 6.25% | 0 | 16 |
| Total cases..... | 46, or 65.71% | 2, or 2.86% | 1, or 1.43% | 21, or 30.00% | 70 |

TABLE 3.—*Patients Treated Conservatively*

| | Cured | Improved | Unimproved | Uncertain | Died | Total Cases |
|--------------------|-----------------|----------|-----------------|----------------|------------------|-------------|
| Spontaneous..... | 2, or 11.77% | 0 | 5, or 29.41% | 1, or 5.88% | 9, or 52.94% | 17 |
| Erosive..... | 1, or 11.11% | 0 | 0 | 0 | 8, or 88.89% | 9 |
| Traumatic..... | 0 | 0 | 1, or 16.67% | 0 | 5, or 83.33% | 6 |
| Arteriovenous..... | 0 | 0 | 0 | 0 | 3, or 100.00% | 3 |
| Total cases..... | 3, or 8.57% | 0 | 6, or 17.14% | 1, or 2.86% | 25, or 71.43% | 35 |

twenty, or 66.67 per cent., died; six, or 20 per cent., were unimproved; in one, or 3.33 per cent., the outcome was not reported, and three, or 10 per cent., recovered. No other argument is needed for recourse to radical arterial surgery than these figures, viz., roughly speaking 70 per cent. recoveries in the operative series against 10 per cent. in the non-operative group, a balance of some 60 per cent. in favor of the former:

or putting it in another way, 25.43 per cent. deaths in the first in comparison with 66.67 per cent. fatalities and 20 per cent. unimprovements in the latter. Until bloodless methods can produce better results, the management of this lesion must remain strictly a surgical problem, and the few cases reported as medical cures should be regarded as a matter of good luck rather than as establishing a sound therapeutic principle for guidance in future emergencies of this character.

Thirty-eight cases were reported as occurring during the last century: spontaneous, twenty-three; erosive, five; traumatic, seven, and arteriovenous, three. Sixty-eight were reported since: spontaneous, fourteen; erosive, thirteen; traumatic, nineteen; arteriovenous, sixteen, and unclassified, one (Table 4).

TABLE 4.—Cases Occurring Prior to and Since 1900

| | Operated On | | | | Not Operated On | | | | Total |
|-------------------|-------------|---------------|-----------------|------|-----------------|-----------------|----------------|------|-------|
| | Cured | Im- proved | Unim- proved | Died | Cured | Unim- proved | Uncer- tain | Died | |
| Spontaneous..... | 10 | 0 | 0 | 7 | 0 | 1 | 0 | 5 | 23 |
| Erosive..... | 1 | 0 | 0 | 2 | 1 | 0 | 0 | 1 | 5 |
| Traumatic..... | 3 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 7 |
| Arteriovenous.... | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 3 |
| Total..... | 15 | 0 | 0 | 11 | 1 | 1 | 0 | 10 | 28 |
| Since 1900 | | | | | | | | | |
| Spontaneous..... | 6 | 0 | 0 | 2 | 2 | 1 | 1 | 4 | 19 |
| Erosive..... | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 7 | 13 |
| Traumatic..... | 9 | 0 | 0 | 0 | 0 | 1 | 0 | 3 | 19 |
| Arteriovenous.... | 12 | 2 | 1 | 0 | 0 | 0 | 0 | 1 | 16 |
| Unclassified..... | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| Total..... | 31 | 2 | 1 | 10 | 2 | 5 | 1 | 16 | 66 |
| Grand total..... | 46 | 2 | 1 | 21 | 3 | 6 | 1 | 26 | 105 |

While conclusions drawn from small series are admittedly often misleading, the difference in the mortality rate of the operative and the nonoperative groups is so peculiarly striking, that one is compelled to attribute the favorable results in the one and the failures in the other to nothing else than the mode of treatment. As approximately three out of four patients coming to operation recover, while four out of five patients treated conservatively die, there should be no hesitancy in the presence of this lesion in recommending an operative attack on the carotid vessels as offering the best, the surest and the quickest prospect of securing permanent relief from the condition.

As a rule the symptoms are frank. On inspection of the throat, there is seen a bulging in the lateral pharyngeal wall. The mass may so encroach on the alimentary tract as to convert the food passageway into a narrow slit. The swelling may be either circumscribed or diffuse. To the touch it is soft and elastic, and pulsates in an expansile manner throughout its entire extent. Externally there may be no evidence of the

disease; or there may be a bogginess; or there may be a distinct lump behind the angle of the jaw. With a stethoscope placed over the swelling a bruit may be heard. Both murmur and pulsation disappear when the common carotid artery is compressed against the vertebral column, to reappear immediately on the reestablishment of the circulation through the affected vessel. With the arrest of the circulation the volume of the mass is greatly diminished. The patient may complain of a roaring in the ear, persistent and severe hemicrania, vertigo and weakness. Swallowing of solids is sometimes impossible and generally accomplished with difficulty. Liquids may be regurgitated through the nose. Dyspnea is a not uncommon complaint. Hoarseness and deviation of the tongue toward the affected side have been observed. Diagnostic puncture has been practiced in obscure cases, but should not be employed unless the patient is so situated that a prompt operation can be done in the event of a rupture through the path of the needle. In an occasional case, the signs of aneurysm are lacking, obscure or atypical. Under such circumstances extraordinary care must be employed to avoid mistakes in diagnosis as an improper interpretation of the condition almost invariably leads to mischievous surgery.

Were this aneurysm more accessible restorative aneurysmorrhaphy would be the ideal treatment. In the arteriovenous type it has been used a few times with entire satisfaction; in the arterial, once by McMullen and Stanton, but the patient died of leakage through the suture line. The operation of choice is ligation of the internal carotid proximal to the aneurysm. If this is impossible, both the common and the external arteries should be ligated and any branches of the latter arising between the site of the ligation and the bifurcation. Before permanently arresting the circulation in the internal carotid artery, the common carotid artery should be temporarily occluded under local anesthesia. Usually a defective cerebral circulation will promptly manifest itself by vertigo or faintness. In the face of these warnings the ligature should be removed without delay.

In this connection I desire to report that the patient operated on by me for an aneurysm of the internal carotid artery in its cervical course still remains completely cured, now more than four years after the operation. In a similar case in which operation was done at the University of Maryland clinic in January, 1915, and which was reported by Shipley and Lynn,³ the patient is symptomatically well at the time this article is being written, a little over ten years since the operation. These results would seem to indicate that stoppage of the circulation through

3. Shipley, A. M., and Lynn, F. S.: Carotid Tumors, *J. A. M. A.* 66:1602 (May 20) 1916.

an internal carotid artery has little if any effect on longevity in those cases in which the patients have weathered successfully the storms incident to such an operation.

SPONTANEOUS TYPE

The cases of spontaneous type number forty-two; twenty-five of the patients were subjected to some form of radical arterial surgery (Table 5), and seventeen were treated conservatively (Table 6). Thirty were women, eleven, men, and in one, the sex was not mentioned. These figures reverse the usual order of events, as aneurysm elsewhere is by far more prevalent in the male than in the female. The ages ranged between $4\frac{3}{4}$ and 76 years. The right side was affected eighteen times; the left, nineteen; the side was not stated in four. Eighteen patients recovered; eighteen died; five were unimproved, and in one, the condition was not mentioned. Twenty-five were operated on, with nine deaths, or a mortality of 36 per cent., and sixteen, or 64 per cent., cures. The operative fatalities were ascribed to hemorrhage three times; to cerebral complications, once; to hemiplegia, twice; to spontaneous rupture of the sac into the mouth and asphyxia on the operating table, once; to sepsis, once; to no assignable cause, once. Seventeen patients were not operated on, with nine, or 52.94 per cent., deaths; two, or 11.77 per cent., were reported as cured; five, or 29.41 per cent., were unimproved when discharged, and in one, or 5.88 per cent., the condition was not given. The deaths in the unoperated on series were attributed to hemorrhage six times; to coma, once; to cerebral symptoms, once; to undetermined causes, once. The imposition of almost unsurmountable anatomic difficulties to direct attack on the sac renders ligation of the common carotid artery alone or in combination, or of the internal carotid artery alone, as the operations of choice. Once only was aneurysmorrhaphy attempted with death of the patient of secondary hemorrhage from a break in the suture line. Peculiar to relate only in a few of these cases was the aneurysm in this series attributed to syphilis. Castex reports two such cases, in both of which he effected cure by antisyphilitic medication and local measures. No other cases were benefited in the least by antisyphilitic therapeutics. In view of the high mortality rate attached to the conservatively treated series, despite the gratifying results obtained by Castex, some form of radical arterial surgery must remain our sheet anchor in the future as in the past.

The vessels ligated and the results were: common carotid, thirteen times, with eight cures and five deaths; common and external carotids, twice, both patients being cured; common and external carotids and superior thyroid, once, with cure; common carotid, repeated with division five months later for return, once, with cure; common, internal

TABLE 5.—*Spontaneous Aneurysms Operated On*

| Case | Author and Reference | Sex*; Age; Side | Dura- tion | Operation Date | Cured | Died; Cause | Remarks |
|------|--|-----------------------|---------------|--|-------|--|---|
| 1 | Cooper: Lectures, Ameri- can Ed 3, 1831, 2:62 | ♂ 50 L | 6 months | Ligation common carotid artery, 6/22/1808 | Yes | | Swelling externally; headache, thumping in the brain; decrease in volume when sac was compressed; regained original size with one contraction of heart; after operation, scarcely an unpleasant symptom; headache relieved; obscure pulsation till September, then felt no more |
| 2 | Dupuytren: Leçons orales de clin. chir., Ed. 2, 1839, 3:56 | ♀ 76 L | 8 years | Ligation common carotid artery, 1/19/1818 | | Yes; 8 days of cerebral complica- tions | Swelling both externally and internally, ovoidal, soft, elastic, expansile throughout, pulsating synchronously with the pulse; beats arrested and lump decreased in size by compressing carotid; overlying skin healthy; dysphagia; mouth opened with difficulty; weakness of left half of tongue; insomnia; after ligation, no return of pulse; necropsy revealed local suppuration, brain negative, calcareous deposits throughout arterial system, aneurysm formed at expense of internal carotid |
| 3 | Porter: Dublin Hosp. Rep. 5:208, 1830; also Dublin J. M. Sc. 17:63, 1840 | ♀ 40 R | 15 years | Ligation common carotid artery, 8/21/1829 | Yes | | Violently pulsating, tense, globular, cervical swelling, first noticed 15 years before as small pulsating lump which at end of 7 years had only attained the size of a small nut; three weeks before struck her neck, then swelling grew rapidly, became tender and sore on touch; right hemiparesis; no pulsation seen in throat; after operation, stiffness, numbness in the right arm, perceptible pulsation in aneurysmal sac; four months postoperative, suppurative sac burst; June, 1830, at her occupation of servant; died, Sept. 7, 1836; necropsy revealed remnant aneurysmal sac internal carotid, with no assignable cause |
| 4 | Porter: Dublin J. M. Sc. 17:86, 1840 | ♂ 38 L | 5 weeks | Ligation common carotid artery, 9/22/1838 | | Yes; sec- ondary hemor- rhage 50th day | Aneurysmal swelling, both internally and externally; intra-oral appearance most alarming, blood column just beneath the mucous membrane, pulsation visible; sac perceived a freely movable, painless, nonpulsating, small, hard kernel near the angle of the jaw; increased steadily in size and began to pulsate; followed by hoarseness for which he sought relief; operation borne well; no more pulsation or pain; swelling became smaller; October 23, change for worse, headache and stiffness in neck; October 27, fluctuating mass at operative site; cough; dyspnea; dysphagia; incised and much pus admixed with blood recovered; October 30, hemorrhage from wound, repeating itself on numerous occasions till November 12, when patient died; necropsy refused |
| 5 | Syme: London & Edin- burgh Month. J. M. Sc. 2:961, 1842 | ♀ 60 | 5 months | Ligation common carotid artery, April, 1842 | | Yes; in 30 hours; no assignable cause | Syme saw patient in consultation; diagnosis was between abscess and aneurysm; Syme learned to latter; necropsy |
| 6 | Duke: Dublin M. Press 19:65, 1848 | ♂ 32 R | 1 year | Ligation common carotid artery | | Yes, in 5 weeks; hem- orrhage | Duke was about to puncture a pharyngeal swelling when he introduced a finger and detected pulsation; he changed his diagnosis to aneurysm; a consultant did not consider the condition so serious, and during a visit in the absence of Duke incised the aneurysm; this was followed by such a severe hemorrhage as to necessitate ligation of the carotid; the operation was followed by slight paralysis |
| 7 | Chassaignac: Bull. Soc. de chir. de Paris 10:88, 1859 | ♂ 26 L | Short time | Ligation common carotid artery, August, 1859 | Yes | | Hemorrhage after puncture of a supposed retropharyngeal abscess, calling for ligation of carotid artery; postoperative aphonia; headache for 24 hours; after one year complete recovery |

| | | | | | | | |
|----|---|---------------|----------|--|-------|--|--|
| 8 | Godfray; M. Times Gaz. 2: 409, 1882 | ♂ 28 R | 5 months | Ligation common carotid artery, 7/30/1876 | Yes | | Gradually increasing swelling in the right side of the neck with pulsation and bruit; lump looked as though it would burst at its hind part; dysphagia; syphilitic taint enlarged again; dysphagia returned; August 20, violent hemorrhage; swelling as large as ever; no pulse or bruit; September 3, aspirated some foul smelling blood; fluctuation of left soft palate; disturbance of speech and deglutition; swelling as to form, free hemorrhage controlled by first operation to recur 1½ hours after patient had been returned to bed; immediately after preliminary operation, aphonia and disturbed respiration; June 10, hemiplegia, same side as operation; died June 12, 1882; necropsy showed extracranial aneurysm internal carotid artery; vagus nerve caught up in primary ligature; hemorrhage at base of brain, right side |
| 9 | Dubruell; Gaz. méd. de Paris 54: 872, 398, 1883 | ♀ 28 L | 6 months | Ligation common carotid artery and later, in the day, ligated the same common carotid, with external carotid, internal carotid, and superior thyroid arteries, 5/29/1883 | Yes | Yes, in 11 days, hemiplegia | Unmarried; no children; no evidence of syphilis; for 10 years a thumping in the region occupied by the lump; ringing in the ear for 4 years; hemicrania; increasing swelling; no pain; no apparent cause; after operation, lump decreased in size almost to the vanishing point; headache relieved |
| 10 | Wyeth New York M. J. 35: 428, 1883 | ♀ 60 L | 10 years | Ligation common carotid, external carotid, and superior thyroid arteries, 1883 | Yes | | Dysphagia; dyspnea; gradually increasing lump in throat, pushing tonsil to midline, pressing carotid, oval in shape, expansile in character; pulsation arrested by compression; after operation, decreased in size, swallowing facilitated; breathing improved, pulsation arrested |
| 11 | Craus; El Genio Medico-Quirurgico 20: 101, 1884 | ♀ 63 R | 2 years | Ligation common carotid artery, 4/12/1884 | Yes | Yes, in about 2 weeks | Large swelling, both internally and externally, growing slowly; pressure on common carotid caused it to shrink; pulsated throughout; bruit present; no assignable cause; 2 weeks after first operation, pulsation reappeared; after second operation, no sound or motion detectable, mass became quite solid; soon afterward she expired week after last ligation |
| 12 | Agnew; Tr. Am. S. A. 4: 252, 1886 | ♀ 5 months | 5 months | Ligation common carotid, superior thyroid and lingual arteries; 2 weeks later, ligation opposite common carotid artery, 1887 | | Yes, on table, of asphyxia from rupture of neck in month | At first diagnosed as abscess, but diagnosis changed to aneurysm on aspiration of internal carotid, sac burst into mouth; temporary ligature which had been placed controlled the further escape of blood, patient died on table of asphyxia from blood aspirated into bronchi, notwithstanding a prompt tracheotomy; diagnosis confirmed by necropsy |
| 13 | Hulbert; St. Louis Cour. Med. 16: 255, 1886 | ♀ 10 R | | Ligation common carotid artery | | | |

TABLE 5.—Spontaneous Aneurysms Operated On—(Continued)

| Case | Author and Reference | Sex*; Age; Side | Dura- tion | Operation Date | Cured | Died; Cause | Remarks |
|------|---|-----------------------|---------------|--|-------|----------------|---|
| 14 | Clementi: Riforma med. 6: 478 (Part 1) 1890 | ♀ 24 L | 1 year | Ligation common carotid artery, 8/3/1889 | Yes | | Ovoid, increasing, pulsating swelling in front of left ear; no cause; internally a bulging pulsating mass, pushing the tonsil toward the right; bruit; compression practised for 26 days without benefit; after 4 months, complete cure; mass much smaller, nonpulsating and left tonsil symmetrical with right |
| 15 | Polak: Weekblad. Nederl. Tijdschr. 36: 1213 (Part 1) 1900 | ♀ 65 L | | Ligation common carotid artery, 9/27/1894; ligation common carotid artery, 4/24/1895 | Yes | | Growing potato sized tumor in left side of neck; buzzing in ear; dizziness; pulsation evident to sight and touch; compression of common carotid caused partial diminution in volume of mass; on right side of neck in course of external carotid a pulsating tumor the size of a hazelnut; diagnosis, bilateral carotid aneurysm, without assignable cause; some weeks later aneurysm of right external carotid artery had about disappeared from self applied compression; 5 months later symptoms had returned in left side of neck; at second operation aneurysm was seen to be arising from internal carotid; some weeks later slight pulsation observed in small, hard mass; 5 years later patient again visited Polak for sleeplessness; annoying thumping in right side of neck; dizziness, ascribed to aneurysm of right external carotid that had gradually attained the size of a hen's egg; March 23, 1900, right common carotid artery ligated; patient, now aged 71, left hospital 10 days later, completely cured |
| 16 | Mayo, O. H.: St. Paul M. J. 1: 751, 1899 | ♀ 23 R | 6 years | Ligation common carotid artery, 8/2/1889 | Yes | | Internally, mass extending to midline; externally, mass behind right jaw; pressure caused it nearly to disappear; pulsation; bruise; right half of tongue atrophied |
| 17 | Heiferich, in Werner: Ztschr. f. Ohrl. 67: 592, 1902 | ♂ 53 R | 8 months | Ligation common and internal carotid arteries, 5/3/1902 | Yes | | Hard, superficially smooth, nonpulsating, nonfluctuating pharyngeal lump; exploratory puncture, no liquid withdrawn; diagnosis, lymphosarcoma; during attempted buccal extirpation, ruptured sac, profuse hemorrhage, oral tamponading, low tracheotomy; postoperative paralysis of hypoglossal nerve and some disturbance to deglutition |
| 18 | Narath: Nederl. Tijdschr. v. Geneesk. 39: 1174, 1903 | ♂ 28 R | 4 weeks | Ligation common, external and inter- nal carotid arter- ies, 2/1/1897 | Yes | | Lump right side of neck of 4 years' duration, attributed to lifting of heavy burden; had taken on increasing activity, causing dysphagia and right hemiparesis; single, had never had syphilis; no syphilitic stigmata; patient living and well 5 years after operation |
| 19 | Van Oampen: Nederl. Tijdschr. v. Geneesk. 39: 1172, 1903 | ♀ 68 R | | Ligation common carotid artery | Yes | | Swelling, both internally and externally; abscess was considered, but pulsation made this supposition untenable; dysphagia; strange feeling in throat; change in voice; after operation, lump disappeared, pulsation arrested, swallowing regained |
| 20 | Jinnu: Rev. de chir., Bu- curest, 13: 596, 1909 | ♀ 23 R | 8 years | Ligation common carotid artery | Yes | | Also an intracranial aneurysm of internal carotid, the sac of which projected into orbit; symptoms, right hemiparesis; noises in head; insomnia; exophthalmos; opistaxis; orbital sac pulsated and had a systolic blow; volume lessened when compressed; fusiform, expansile swelling in neck with systolic blow; volume much diminished on compression of common carotid; on attempt to enucleate the cephalic aneurysm, its sac ruptured, controlled by inserting finger into rent until common carotid could be ligated; bleeding recurred when finger was withdrawn but in considerably less amount and was entirely checked by invaginating sac with a sterile cork stopper placed in hole and held in position by suturing overlying skin; at time of report the buried cork had been borne well; although no history of syphilis could be obtained, patient was given antisyphilitic medication |

21 McMullen and Stanton:
Ann. Surg. 51: 76, 1910

♀ 60
R

1 year

Endo-aneurys-
morrhaphy,
12/20/1908

....

Yes, In 20
days; sec-
ondary hem-
orrhage

22 Perthes, in
Koppler: In-
augural Disser-
tation, 1910
University of
Leipzig, 44
L

3 months

Ligation common,
external and inter-
nal carotid arter-
ies; extirpa-
tion of sac,
7/19/1909

....

Yes, July
20, 1909;
hemipar-
esis

23 Moser: Inaugural Disser-
tation, Kaiser Wilhelm's
University, Strasburg, 1911, p. 7
♀ 60
R

6 days

Ligation common
and internal caro-
tid arteries; extir-
pation of sac,
7/7/1910

Yes

24 Shipley and Lynn: J. A.
M. A. 66: 162, 1916
♀ 41
L

2 years

Ligation common
and external caro-
tid arteries,
1/31/1915

Yes

25 Winslow: Ann. Surg. 75:
634, 1922
♀ 48
R

9 months

Ligation common
and external caro-
tid arteries,
2/1/1921

Yes

Painless, pulsating, steadily developing mass in right side of neck; no cerebral symptoms; no specific history; swelling in throat; 15 days after operation, patient discharged as cured, to return 3 days later with hematoma under scar; this was arrested on the twentieth postoperative day, followed by a copious hemorrhage in throat; dyspnea; no miscarriages; fullness in neck for 3 months; sticky sensation in left side of pharynx and larynx; which she consulted Lohse, who detected a firm, elastic, pulsating mass in the neck; no palpable arteries; pharyngeal mass was covered with a normal mucous membrane, was firm and elastic in consistency, and pul- sation; aphasia; paralysis of right arm and right half of face; fully conscious; no left anterior cerebral artery and its branches; softening of anterior; thrombosis of left carotid; walls of aneurysm showed no calcareous deposits; Patient had 2 pregnancies; had lifted a bundle of wet grass to her head, next day roaring in right ear and succeeding day lump in right side of neck; no pain; with the radial pulse, size of hen's egg; thrill; bruit; disappeared synchronously removed; nothing abnormal in mouth; after operation, severe pain right side of face; dysphagia, no speech, paralysis right arm and leg; and lower left side of head, impelliment to food condition discharged in good condition and with bulging in left side of throat; increasing dyspnea; dysphagia, and pulsated throughout; bruit heard; some months after operation, patient escaped; lump gradually grew larger, causing dysphagia for a few days; July 21, 1922, she was entirely well, could swallow and thumping in head had disappeared; said she did not have syphilis; Wassermann test negative; twenty-ray examination of cervical vertebrae negative.

* In this and the following tables, ♂ Indefinite male; ♀, female

TABLE 6.—Spontaneous Aneurysms Not Operated On

| Case | Author and Reference | Sex; Age; Side | Duration | Cured | Died; Cause | Remarks |
|------|--|-----------------|------------|------------|-----------------------------------|--|
| 26 | Perier: Rec. de m ^é m. de m ^é d. et de chir. et de phur. militaires 14 : 311, 1881 | ♂ 19 | 14 days | | Yes, soon; hemorrhage | Dec. 4, 1848, complained of pain in left temporomaxillary joint, but no swelling or change in color of skin; however, movements of the articulation were embarrassed and limited; pain and rumbling in left ear; at this time nothing abnormal in mouth; December 7, boggingness behind angle of jaw, which could scarcely be opened sufficiently to permit introduction of little finger; velum of palate was pushed by a swelling far toward right; dysphagia; external tumefaction, deep seated, nonpainful on pressure and obscurely pulsating; December 9, hemorrhage from the mouth and nose, repeated frequently; though symptoms were obscure aneurysm of internal carotid was diagnosed; December 18, while Reamier was introducing a finger into mouth, sac ruptured and patient soon died; necropsy confirmed diagnosis |
| 27 | Pircher: Wien. med. Wochenschr. 12 : 553, 556, 1862 | ♀ 8 L | 1 month | | Yes, in one month; hemorrhage | Condition diagnosed as abscess; external swelling; could not open mouth; made an incision, but did not reach abscess; consultants were of opinion that lesion was inflammatory; on their advice inserted a trocar again, without result; child died Feb. 7, 1862, of hemorrhage into mouth; necropsy revealed aneurysm of internal carotid artery |
| 28 | Coomes: M. Herald 7 : 503, 1885 | ♀ Woman L | 10 days | | Yes, in 10 days; hemorrhage | White courtesan, first seen Dec. 14, 1885, for hemorrhage from mouth and nose; said she had never had syphilis, no stigmas of syphilis present; pain in left ear; some puffiness of neck and a protrusion into pharynx which had appearance of an abscess; Coomes had proposed putting a knife into it, but sticking a finger into the mouth, he felt its surface hard and unyielding; the cutting was therefore abandoned; externally no pulsation felt; only after several days' observation was pulsation detected, both internally and externally; also a lump both on inside and outside of mouth; bleeding recurred at intervals until December 23, when patient died; necropsy revealed aneurysm of internal carotid swelling in left side of pharynx and extending to median line; pulsation; bruit; compression of common carotid lessened its volume; treated on two separate occasions by digital compression to common carotid; after apparently having been cured, he experienced severe pain in head and toppled over dead; necropsy could determine no definite cause for death |
| 29 | Vunder Veer: Tr. Am. S. A. 4 : 263, 1886 | ♂ 40 L | 2 months | | Yes, in about 3 months; suddenly | Swelling in left side of pharynx and extending to median line; pulsation; bruit; compression of common carotid lessened its volume; treated on two separate occasions by digital compression to common carotid; after apparently having been cured, he experienced severe pain in head and toppled over dead; necropsy could determine no definite cause for death |
| 30 | Richardson: J. A. M. A. 15 : 180, 1890 | ♀ 35 R | Short time | Unimproved | | Bulging, pulsating mass in right lateral pharyngeal wall; bruit; reached to midline; compression of common carotid caused decrease in its volume and arrested pulsation; patient was annoyed by thumping; blood seemed to be just beneath mucous membrane and it appeared with each pulsation that the swelling must rupture; patient drifted out of sight without having received any treatment |
| 31 | Edmunds: Tr. Path. Soc. London 43 : 42, 1891 | ♂ 36 R | 1 month | | Yes, in 12 days; coma | Pulsating tumor in right side of neck, rapidly increasing in size; no pain or discomfort; giddiness; syphilis 12 years before; examination caused attacks of giddiness and fainting; so operation was rejected; necropsy: aneurysm of internal carotid close to its origin |
| 32 | Minichi: Pest. med.-chir. Presse 38 : 765, 1901 | ♀ 30 | 3 weeks | | Yes, in 3 days; hemorrhage | Intrabuccal swelling; dyspnea; mistaking swelling for an abscess, her physician made an incision into it, obtaining pure blood; hemorrhage arrested with difficulty; followed two days later by a mortal hemorrhage; neither pulsation nor fluctuation; necropsy: aneurysm of internal carotid, projecting into pharynx; in discussion Ling cites a similar case observed in 1894 which ruptured spontaneously, but supplies no data |
| 33 | Texier: Bull. m ^é d. Paris 21 : 593, 1907 | ♀ 74 L | 1 year | | Yes, in 7 days, cerebral symptoms | Swelling occupying entire left half of pharynx and pushing tonsil and uvula to right; externally no suggestion of swelling; mass in mouth did not pulsate and as its upper part was soft it was thought to be an abscess; trocar stuck into it for diagnostic purposes obtained pure blood; diagnosis: aneurysm of internal carotid or a vascular tumor; necropsy: aneurysm of internal carotid artery, without assignable cause; coma attributed to cerebral edema |
| 34 | Texier: Bull. m ^é d. Paris 21 : 593, 1907 | ♀ 47 L | Short time | Unimproved | | Swelling in throat; occasional sensation of an obstacle in throat; dyspnea at night; no noises in ear; surface of mass smooth; pulsated at its lower end only; soft bruit, both internally and externally; iodid of potassium was advised and patient requested to return later, reserving till then advisability of ligating carotid artery |
| 35 | Texier and Levesque: Gaz. m ^é d. de Nantes 28 : 466, 1910 | ♀ 42 L | | Unimproved | | Swelling in left wall of pharynx; patient felt pulsation corresponding to beats of pulse in the half of head and neck of diseased side; externally no appreciable fulness; not tender to touch; not expansile; not pulsatile; no fluctuation; no operation; antisyphilitic treatment |

- | No. | Author | Year | Age | Sex | Side | Duration | Result | Notes |
|-----|--|------|-----------|-----|---------------|------------|--------|---|
| 36 | Wagner, in Keppler; Inaugural Dissertation, University of Leipzig, 1910, p. 14 | | Child | | | | | Yes; hemorrhage, spontaneous rupture of sac |
| 37 | Lisbault and Daudin-Clavaud; Arch. gén. de chir. de Paris S: 1436, 1912 | | ♀ 7½ R | | 18 months | Unimproved | | |
| 38 | Veiehl; Casop. lékař. Cesk. Prague 52: 975, 1913 | | ♂ 4¾ R | | 3 weeks | | | Yes, Jan. 4, 1913; hemorrhage from mouth |
| 39 | Cannuyt; Arch. Franco-Belges de Chir. 27: 404, 1921-1922 | | ♀ ES L | | | Unimproved | | |
| 40 | Portmann and Dupouy; Arch. méd. belges 76: 97, 1923 | | ♂ 6S L | | Uncertain | | | |
| 41 | Castex; Ann. de méd. 10: 138, 1924 | | ♀ 46 L | | | Yes | | |
| 42 | Castex; Ann. de méd. 10: 138, 1924 | | ♀ 45 R | | About 6 years | Yes | | |

and external carotids, once, with cure; common and internal carotids, once, with cure; common, external and internal carotids with extirpation of sac, once, with death; common and internal carotids, above and below sac and extirpation of sac, once, with cure; common carotid, superior thyroid, lingual and opposite common carotid, once, with death; common carotid, repeated later the same day and in addition the external and internal carotids and superior thyroid, once, with death; common carotid and plugging of hole in an orbital sac with a piece of cork, opened accidentally on account of two aneurysms, one in the neck, and one partly within the cranium and partly orbital, once, with cure.

Chassaignac lanced a retropharyngeal swelling for abscess, but fortunately cured the patient by ligation of the common carotid artery. Dubrueil mistook a pharyngeal swelling for sarcoma and during an attempt at enucleation tore the sac wall. The escaping blood was arrested by a ligation of the common, internal and external carotid and the superior thyroid arteries, but the patient died fourteen days later of hemiplegia. Helferich had the same accident befall him, but fortunately saved his patient by a ligation of the common and internal carotid arteries. Hulbert was saved a similar fate when he inserted a needle into the sac and withdrew pure blood. Though Agnew ligated both common carotid arteries and the superior thyroid and lingual arteries on the side of the lesion, the current was reestablished in the internal carotid, with rupture of the sac and death from sepsis. The case of Jianu is extraordinary. There were two aneurysms in the course of the internal carotid, one cervical and the second projecting from within the cranium into the orbit and presenting at the naso-orbital junction. While attempting to enucleate the latter, Jianu tore the sac wall. To control the escaping blood he inserted a finger into the hole and then proceeded to ligate the common carotid. As there was still some oozing from the rent when this was accomplished, Jianu invaginated the sac wall with a piece of cork and sutured the skin over it to keep it in place. Happily the patient recovered.

Radical artery surgery needs no further brief than 64 per cent. cures against 11.77 per cent. when other tactics are employed. Another and important lesson taught by these studies is that in the presence of a unilateral pharyngeal swelling before puncture one should listen, feel and touch. Among others Minich reported a case in which an attending physician had lanced for abscess. With difficulty the hemorrhage was checked but two days later the bleeding recurred and could not be arrested. In this case neither pulsation nor fluctuation was felt. Wagner was spared a like experience by forgetting to take along his instruments. When he returned the next morning he was told that the patient had died during the night of hemorrhage from the mouth.

Vander Veer believed he had effected a cure by digital compression of the common carotid artery, but three months after the initiation of the treatment the man fell dead. Edmunds refrained from operation because examination caused giddy spells and faintness. The cases of Perier, Pircher, Coomes and Wagner are a grim reminder that death ever threatens from spontaneous rupture into the mouth when the proper surgical measures are withheld.

Though not eligible for tabulation, the following cases merit notice here. Walsham⁴ reports a case of aneurysm involving all three carotids. The patient was a man, aged 49, with a nonpulsatile swelling in the right side of the neck of six years' duration. The growth was the size of a cricket ball, globular, hard, and extended from the jaw almost to the clavicle. Until operation, it was thought to be a malignant tumor. A dry tap was made. There was no bulging in the throat, no dyspnea, and no dysphagia. The operation performed, Dec. 5, 1895, consisted of ligation of the common, external and internal carotids with enucleation of the sac. The patient was cured. Deaver⁵ cites a similar experience. The patient, a man, aged 46, had had a swelling in the right side of the neck for twenty years. All three carotids were involved in the dilatation. The common carotid artery was tied successfully, Sept. 25, 1888. Prosser⁶ and Langenbuch⁷ report cases that have been cited as aneurysm of the internal carotid artery, but owing to insufficient evidence these have had to be omitted from my series. Prosser's patient, a woman, aged 70, had had a pulsating tumor in front of the right ear for a number of years. Pulsation disappeared after ligation of the common carotid artery and the swelling diminished, but before very long reappeared. Langenbuch's patient was a woman, aged 66, with a pulsating mass in the left lateral portion of the neck, with an audible souffle. Ligation was not practiced because of the age of the patient. An attempt was made merely to narrow the lumen of the vessel by means of a silk ligature so as to lessen but not interrupt the current of blood. Following this procedure the pain and pulsation were less intense.

Ott⁸ cites the case of a woman, aged 26, who went to the Mayo Clinic for consultation, Feb. 14, 1913. Six years before she had had bleeding from the right ear. One year afterward she was seized with severe throbbing, pain in the head, dizziness and bleeding from the ear

4. Walsham: *Proc. Roy. M. & S. Soc.* 12:71, 1899; also *Tr. M. & S. Soc.*, London 82:223, 1899.

5. Deaver: *Univ. M. Mag.* 1:340, 1889.

6. Prosser: *Brit. M. J.* 1:530, 1897.

7. Langenbuch: *Mercredi méd.* 3:21, 1892.

8. Ott, W. O.: *Results of Twenty-One Cases of Surgical Treatment of Aneurysm*, *Ann. Surg.* 74:517-522, 1921.

of more or less intensity. Examination revealed a pulsating tumor in front of the right ear and another in the left submaxillary space. The patient could scarcely open her mouth. A diagnosis was made of aneurysm of the right external carotid artery for the one lump and of aneurysm of the internal carotid artery for the mass on the opposite side. The right external carotid artery and internal jugular vein were ligated, Feb. 20, 1919. Six days later the left common carotid artery was tied just below its bifurcation for an aneurysm which apparently involved both the internal and the external carotids. The patient reported two years later that the aneurysm had shown no signs of recurrence.

Meyer⁹ reports what he believes eight examples of aneurysm of the extracranial portion of the internal carotid artery. All the observations were made at necropsy on mentally deranged patients. From the solitary illustration featuring the article and the subject matter of the text, the condition appears rather to have been a slight thickening of the arterial wall at its point of origin. Shaefer,¹⁰ following the lead of Meyer, describes the same condition as aneurysm of the internal carotid artery. Macfarlan¹¹ does not offer sufficient evidence to justify the acceptance of his cases as aneurysms of the cervical portion of the internal carotid artery. The first observation concerned a woman, aged 58, who sought relief for a whistling noise in the right ear of two years' duration, which kept her awake at night. Listening in the region of the right ear Macfarlan heard a slight systolic murmur, synchronous with the pulse. The author thought the condition due to an extracranial aneurysm of the internal carotid located near the base of the skull. The second patient, a woman, aged 62, complained of ear noises. These became gradually worse and prevented sleep. May 8, 1920, a slight pulsation was seen in the upper part of the neck in front of the left sternocleidomastoid muscle. When one listened over this area with a stethoscope a faint bruit was heard. It was blowing and in unison with the pulse. The disability was attributed to an aneurysm in the upper portion of the common carotid artery or at the beginning of the internal carotid. Though wanting in data, the case of Hodgson, related by Partridge¹² in the discussion on Liston's paper, has every appearance of being a genuine aneurysm of the internal carotid. The patient was a child, aged 9 years, with involvement of all three coats of the artery.

9. Meyer, Ludwig: Ueber aneurysmatische Veraenderungen der Carotis interna Geisterkranker, *Arch. f. Psychiat.* 6:84, 1875.

10. Shaefer: *Allg. Ztschr. f. Psychiat.* 34:483, 1887.

11. Macfarlan: *J. Ophth., Otol. & Laryngol.* 24:390, 1920.

12. Partridge: *Lancet* 1:866, 1842.

The cases of Hunter and Marchal, cited by Wyeth,¹³ though very suggestive, could not be confirmed. Hunter's patient was a woman, aged 60, with an aneurysm in the mouth, for which ligation of the common carotid was practiced, followed four days later by death. Marchal opened an aneurysm for an abscess. To arrest the bleeding he ligated first the external carotid artery but did not bring the hemorrhage under control until the common carotid artery also was tied; the patient died, however, six days afterward of cerebral complications. The patient was a man, aged 25, with a swelling in the left side of the throat of two months' duration.¹⁴

FROSTY TYPE

Altogether I could discover the case reports of only eighteen examples of this aneurysm published in the domestic and foreign literatures. The smallness of the number is undoubtedly due to the hesitancy of physicians to report their failures, notwithstanding that equally as important lessons are to be learned from mistakes as from successes. Of all the varieties of carotid aneurysm, this is by far the most weird, the most confusing, the most treacherous. The series, as a whole, is a pathetic exhibition of colossal blunders in diagnosis and in treatment.

Of the eighteen patients, twelve died and six recovered. Twelve were males; five females, and the sex of one was not mentioned. Eleven were twenty or under, five over twenty. The ages varied between 11 months and 60 years. In one instance the age was not recorded. The left side was affected twelve times; the right, six. Radical operation was done nine times (Table 7). Of these patients, five, or 55.5 per cent., recovered, and four, or 44.5 per cent., died. The deaths were attributed to hemorrhage twice; to sepsis, exhaustion and hemorrhage, once, and to pneumonia, once. Of the nine cases not subjected to arterial surgery, one, or 11.2 per cent., recovered and eight, or 88.8 per cent., died (Table 8). The causes of death in the unoperative series were spontaneous hemorrhage, four times; anesthesia, once, and hemorrhage from puncture of the sac, three times. Though operative relief holds out the prospect of only 55.5 per cent. cures, this percentage contrasts more than favorably with 11.2 per cent. cures when a watchful policy is adopted. The vessels ligated were: common carotid, five times, with two cures and three deaths; common carotid and splitting of sac, once, with cure; common carotid and internal jugular vein, once, with death; common carotid and division, later internal and external carotids and extirpation of sac, once, with cure, and internal carotid, once, with cure.

A spontaneous cure was reported by Lyot and Petit. The patient had had scarlet fever, followed by a severe inflammation of the throat,

13. Wyeth: *Tr. A. M. A.* 29:56-58 (Appendix), 1878.

14. Norris: *Am. J. M. Sc.* 14:14, 1847.

TABLE 7.—*Erosive Aneurysms Operated On*

| Case | Author and Reference | Sex; Age; Side | Duration | Operation Date | Cured | Died; Cause | Remarks |
|------|---|----------------|----------|--|-------|-------------------------------|--|
| 1 | Linton: Lancet 1842 | ♂ 18; R | 2 months | Ligation common carotid artery, 1841 | | Yes, in 15 days; hemorrhage | Six years before had scarlet fever; two months before, cough, fever and small swelling beneath right ear; at first slow growing; 3 days before admission increased enormously in volume; projected into mouth between palatal arches and interfered with both deglutition and respiration; indistinctly fluctuating; intra-orally no pulsation; punctured for an abscess, with rush of blood instead of pus escaping; hole closed with hairlip pins and twisted silk; next day, artery ligated; 13 days after operation, hemorrhage from neck, repeated six times; patient died, Nov. 5, 1841, in collapse; necropsy: aneurysm extracranial part internal carotid artery. |
| 2 | Postembelski: med. G. (Part 1) 1890 | ♂ 470, 1 | | Ligation common carotid artery and incision of sac, 1890 | Yes | | Patient seen a month prior, had false aneurysm, complaining an abscessed tonsil; postoperative course uneventful; case reported at meeting of Association of Italian Surgeons, Florence, 1890 |
| 3 | Barthel, in Henson: Birmingham M. Rev. 304, 1891 | ♂ 20; 1 | 10 days | Ligation common carotid artery, 7/3/1890 | | Yes, July 6, 1890; hemorrhage | Quinsy, June 23, 1890; 3 days before admission, profuse hemorrhage from mouth and nose, controlled by nasal packing; repented, July 2 and 3, with some oozing from ear also; July 2, swelling noticed in left parotid region; taken for an inflamed gland; on admission, blood trickling from left ear and nostrils; large ill defined swelling in left side of neck, pulsating in unison with heart; mouth could be opened only with difficulty; left tonsil, pushed across midline; swelling soft and fluctuant; mucous membrane, tense and shiny and pulsed asynchronously with swelling on outside and in expansive manner; no bruit or thrill; all pulsation arrested by pressure on common carotid; during induction of anesthesia breathing ceased, for which Hiasian did a tracheotomy; all pulsation ceased after artery was tied; aneurysm shrank considerably, but patient died, July 6; necropsy: aneurysm internal carotid artery which had ruptured into mouth |
| 4 | Wulff: Munchen. Wehnschr. 47: 657, 1900 | ♀ 8; 1 | 2 months | Ligation common carotid artery, 2/4/1900 | Yes | | Pollicular tonsillitis; shortly thereafter swelling in left tonsillar region; lanced with the recovery of blood only; middle of January, 1900, lump in throat, pulsating to both sight and touch; suspecting aneurysm, author inserted a needle; blood only aspirated; at first treated by compression, but without success; after ligation all motion in sac ceased, never to return, but clot in sac eventually suppurated, necessitating incision |
| 5 | Zamboni, in del Fabro: 13th Cong. int. de med., Paris, sec. de chir. gén. 10: 546, 1900 | ♀ 60; R | 3 years | Ligation internal carotid artery, 1900 | Yes | | No history of syphilis; influenza 3 years before, month later sensation of a lump in throat, oppressed breathing, hoarseness; one year prior to admission, noticed mass in throat; dysphagia; fever; vertigo; unconsciousness; convulsions; condition diagnosed abscess; incision advised but rejected by patient; became worse; needle inserted and blood aspirated; as needle tract continued to trickle blood, patient visited author, who could discover nothing abnormal except roundish tumor in right tonsillar region; uvula pushed well to left; pulsation visible; finger in mouth felt round, stiff, elastic, smooth, fluctuating and strongly pulsating mass which caused muffling of voice; diagnosis, aneurysm; patient expected no inconvenience from ligation; 2 months later tumor was reduced in volume, sac firm, voice clear and deglutition improved |

Ten years before, patient noticed slowly growing lump in left side of neck, which 4 weeks previous to admission had begun to increase rapidly in size; mouth opened with difficulty; dysphagia; dyspnea; pain; paralysis of the left hypoglossal and recurrent laryngeal nerves; Dec. 11, 1902, suddenly ceased breathing; for resuscitation tracheotomy done; no ill effects from ligation of common carotid; lump became smaller; no reappearance of pulse, but dysphagia persisted, so second operation was done, April 4, 1903, incision unchanged; hypoglossal still paralyzed; no swelling inside or outside throat; no bruit or pulsation; originally there was a swelling, both internally and externally; bruit and expansive pulsation synchronous with the beats of the arteries.

Sensation of foreign body in right side of throat for a year with no pain, dysphagia or difficulty in speaking; on inspection, spheroidal tumor, with smooth, glistening surface pushing right tonsil quite to uvula; at first glance would have been mistaken for peritonsillar abscess, but its long duration, absence of pain, and lack of inflammatory signs were against such a diagnosis; besides swelling was actively pulsating, movements being rhythmical with radial pulse; she had had fainting in right ear; accordingly, diagnosis was made of aneurysm of one of carotids, most likely internal; a colleague suggested that a trocar be inserted to verify diagnosis, a procedure which Helman deemed neither expedient nor safe; ligation of common carotid advised, but rejected by patient; loud murmur corresponding in time to heart beat heard; blow much diminished by pressing on aneurysm carotid; given potassium iodid; Helman learned several months later that patient had undergone operation at Warsaw and an aneurysm of internal carotid artery had been found; according to Helman, a colleague in dispensary had almost observed this aneurysm for abscess; he had sent the woman to clinic for demonstration, having advised her to return for puncture; as patient gave history of sore throat some months before, author believed it of erosive rather than spontaneous origin.

Incurred in course of acute bilateral tonsillitis; high fever; large mass under angle of left jaw; on seventh day profuse hemorrhage from mouth, necessitating ligation of carotid artery; as internal jugular vein was injured in course of operation, it was ligatured and resected; necrosis; aneurysm of internal carotid artery.

Had had septic sore throat; left sublingual glands suppurated and were lanced eight days before admission; hemorrhage from drainage tract, 3 days before, retarded day of entrance, Jan. 20, 1903; immobility put under gas and glands resected; when throat was examined, it was found that hemorrhage was from aneurysm of internal carotid artery; swelling in left pharyngeal wall as large as a bean; elastic and pulsating; compression of common carotid raised pulse to disappear; after the girl was returned to bed, tracheal dyspnea arose from pressure of ligation on larynx necessitating a precautionary tracheotomy; 3 months later she was perfectly well; there had been no return of pulse in temporal artery.

| | | | | | | | | | |
|---|---|--------|----------|---|------|-------|-------|--|--|
| 6 | Bruns, in Blauel: Beitr. z. klin. Ohrr. 35: 620, 1903 | ♀ 59 L | 10 years | Ligation and division common carotid artery, 12/16/1902; ligation internal and external carotid arteries, suc. 4/4/1903 | Yes | | | Yes: par-pneumonia | <p>Ten years before, patient noticed slowly growing lump in left side of neck, which 4 weeks previous to admission had begun to increase rapidly in size; mouth opened with difficulty; dysphagia; dyspnea; pain; paralysis of the left hypoglossal and recurrent laryngeal nerves; Dec. 11, 1902, suddenly ceased breathing; for resuscitation tracheotomy done; no ill effects from ligation of common carotid; lump became smaller; no reappearance of pulse, but dysphagia persisted, so second operation was done, April 4, 1903, incision unchanged; hypoglossal still paralyzed; no swelling inside or outside throat; no bruit or pulsation; originally there was a swelling, both internally and externally; bruit and expansive pulsation synchronous with the beats of the arteries.</p> <p>Sensation of foreign body in right side of throat for a year with no pain, dysphagia or difficulty in speaking; on inspection, spheroidal tumor, with smooth, glistening surface pushing right tonsil quite to uvula; at first glance would have been mistaken for peritonsillar abscess, but its long duration, absence of pain, and lack of inflammatory signs were against such a diagnosis; besides swelling was actively pulsating, movements being rhythmical with radial pulse; she had had fainting in right ear; accordingly, diagnosis was made of aneurysm of one of carotids, most likely internal; a colleague suggested that a trocar be inserted to verify diagnosis, a procedure which Helman deemed neither expedient nor safe; ligation of common carotid advised, but rejected by patient; loud murmur corresponding in time to heart beat heard; blow much diminished by pressing on aneurysm carotid; given potassium iodid; Helman learned several months later that patient had undergone operation at Warsaw and an aneurysm of internal carotid artery had been found; according to Helman, a colleague in dispensary had almost observed this aneurysm for abscess; he had sent the woman to clinic for demonstration, having advised her to return for puncture; as patient gave history of sore throat some months before, author believed it of erosive rather than spontaneous origin.</p> <p>Incurred in course of acute bilateral tonsillitis; high fever; large mass under angle of left jaw; on seventh day profuse hemorrhage from mouth, necessitating ligation of carotid artery; as internal jugular vein was injured in course of operation, it was ligatured and resected; necrosis; aneurysm of internal carotid artery.</p> |
| 7 | Helman: Ushn., Gorlov. i Nosov. Bolozn. 6: 76, 1911; also Medyevna, kronika lekarska 44: 681, 703, 1909 | ♀ 34 R | 1 year | Ligation common carotid artery, about 1910 | | | | Yes: par-pneumonia | <p>Had had septic sore throat; left sublingual glands suppurated and were lanced eight days before admission; hemorrhage from drainage tract, 3 days before, retarded day of entrance, Jan. 20, 1903; immobility put under gas and glands resected; when throat was examined, it was found that hemorrhage was from aneurysm of internal carotid artery; swelling in left pharyngeal wall as large as a bean; elastic and pulsating; compression of common carotid raised pulse to disappear; after the girl was returned to bed, tracheal dyspnea arose from pressure of ligation on larynx necessitating a precautionary tracheotomy; 3 months later she was perfectly well; there had been no return of pulse in temporal artery.</p> |
| 8 | Marschik, in Klarfeld: Wien. klin. Wchnschr. 28: 1861, 1915 | ♂ 18 L | 7 days | Ligation common carotid artery and internal jugular vein | | | | Yes: 12 hours after operation, sepsis, ex-haustion, hemorrhage | <p>Incurred in course of acute bilateral tonsillitis; high fever; large mass under angle of left jaw; on seventh day profuse hemorrhage from mouth, necessitating ligation of carotid artery; as internal jugular vein was injured in course of operation, it was ligatured and resected; necrosis; aneurysm of internal carotid artery.</p> |
| 9 | Ransohoff: Ann. Surg. 68: 152, 1918 | ♀ 10 L | 1 week | Ligation common carotid artery, 1/20/1915 | Yes | | | | <p>Had had septic sore throat; left sublingual glands suppurated and were lanced eight days before admission; hemorrhage from drainage tract, 3 days before, retarded day of entrance, Jan. 20, 1903; immobility put under gas and glands resected; when throat was examined, it was found that hemorrhage was from aneurysm of internal carotid artery; swelling in left pharyngeal wall as large as a bean; elastic and pulsating; compression of common carotid raised pulse to disappear; after the girl was returned to bed, tracheal dyspnea arose from pressure of ligation on larynx necessitating a precautionary tracheotomy; 3 months later she was perfectly well; there had been no return of pulse in temporal artery.</p> |

TABLE 8.—*Erosive Aneurysms Not Operated On*

| Case | Author and Reference | Sex; Age; Side | Duration | Cured | Died; Cause | Remarks |
|------|---|----------------|-----------|------------------|--|--|
| 10 | Neuffer: Ztschr. f. Wundärztze u. Geburtsh. 4: 266, 1832 | ♂ 13 L | | | Yes, in 2 days; hemorrhage | Had had angina tonsillaris in fall of 1831; food passage narrowed; dysphagia; as disease progressed jaws became fixed and could scarcely be opened; external remedies employed fruitfully and on twelfth day of disease patient had profuse hemorrhage from mouth; repeated on the thirteenth day, with fatal ending; necropsy: aneurysm of internal carotid with opening into mouth |
| 11 | Lyon and Petit: Gaz. méd. de Paris 1: 159, 1837 | ♀ 19 L | 1½ months | Yes; spontaneous | | Had had scarlet fever complicated by severe inflammation of throat, and later walnut sized growth that pulsed energetically, but could be emptied by compression; on puncture, pure blood obtained; though patient received no treatment, lump had about disappeared in 3 months; symptoms; lump both on inside and outside of pharynx; expansive pulsation; dysphagia; elastic uniform consistency; aspiration of blood; reduction in size by pressure on carotid; systolic bruit, would seem to clinch diagnosis; ligation not done on account of the poor condition of patient |
| 12 | Johnson: Tr. Am. Laryngol., Rhinol. & Otol. Soc. 7: 229, 1910 | ♂ 4 L | 10 days | | Yes; 5 months hemorrhage | Gave history of sore throat for 10 days, fever, pain, and swelling in tonsillar region; had been seen by number of physicians, most of whom believed condition a peritonsillar abscess; incision contemplated, but not undertaken on account of unripeness of patient; midwife had even attempted to scratch hole in it with finger nail; soon ear began to discharge; first seen by Johnson, March 15, 1900, in consultation with another physician who thought swelling an abscess; auditory canal now completely filled by pulsating mass; also present a tense swelling in upper part of neck in which no pulsation could be seen or felt or bruit heard; internally, a tumor occupying left tonsillar region, tense, red and easily compressible; diagnosis: aneurysm of internal carotid; patient not seen again until June 11; patient now dyspneic, drowsy, stupid; mass much larger; tonsil removed and tracheotomy done; child did fairly well until Sept. 7, 1900, when sac ruptured into mouth and continued to ooze until September 11, when child died |
| 13 | Velebl: Ousop. lek. česk. 52: 976, 1913 | ♂ 2½ R | | | Yes, June 13, 1909; hemorrhage from puncture | Brought to hospital, June 13, 1909, for dyspnea and dysphagia; on examination, found bulging, fluctuating mass in oropharynx which was taken for an abscess; swelling bluntly punctured with forceps; instead of pus escaping, stream of blood spurted out through mouth and nose; packing proved futile and child died in few minutes; necropsy showed right suppurative otitis media, right purulent mastoiditis with necrosis in vicinity of carotid canal, aneurysm of internal carotid in neck, with stoma into mouth; on pressure yellowish exudate was forced out of crypts of slightly hypertrophied tonsils; cervical glands swollen and hard; no cause assigned by author, but probably erosive |

| | | | | | | |
|----|---|--------|---------|------|---|--|
| 16 | Hirsch, Monstsch. 4. Otolith. 484-489, 1914 | ♂ L | 3 years | | Yes; on the operating table, from anesthetic (chloroform) | <p>Following attack of scarlet fever, bleeding from mouth and ear; below left ear firm, mass extending to midline; Hirsch attributed condition to middle ear disease and had decided to do a radical mastoidectomy; while going under anesthesia child caused breathing rapid laryngotomy of no avail; no reason assigned for lesion; no Wassermann test permitted; fearing necropsy would not be permitted author made incision in neck aneurysm of internal carotid discovered</p> <p>When seen in May, 1913, child had had scarlet fever for 3 weeks and for some days increasing dysphagia and dyspnea; diffuse, palpable, throat deeply injected but without visible arching deep in left retropharyngeal region, fluctuating mass size of hazelnut; diagnosis, abscess of lymphatic; finger inserted to control hemorrhage and tracheotomy done, pre-operative surgery could be accomplished; necropsy showed aneurysm of internal carotid, the toxins of which had softened walls of diseased vessel</p> <p>Soldier, never at front, May 12, 1917, without ascertainable cause, had profuse hemorrhage from nose and mouth; arrested with tampons; on their removal next day there was active bleeding for which man was transferred to care of Beck; examination of throat revealed only few raw spots in mucous membrane of left side; May 17, 1917, uncontrollable carotid artery, size of walnut and fused with tuberculous gland; in oropharynx was aneurysm no bulging in pharyngeal wall; failure of aneurysm to point in throat ascribed to its being forced backward by contracting lymphatic gland; overlooking of pulsation attributed to same cause; diagnosis made at necropsy</p> |
| 17 | Pisatelli, Polliclinico, sez. Prat. 257-475, 1918 | ♂ R | | | Yes; repeated hemorrhages from spontaneous rupture | <p>Soldier, May 8, 1917, introduced nitric acid into right ear; 17 days later facial paralysis developed, and 8 days later he had nosebleed; night of November 25-26, profuse hemorrhage caused death; necropsy: aneurysm of internal carotid and similar condition in internal jugular vein, both of which had burst; also purulent meningitis; condition not recognized until necropsy; case illustrates danger of inflammation extending through bony walls of ear and so weakening walls of contiguous vessels as to permit formation of aneurysm</p> |
| 18 | Schlagenhafter, allg. Path. u. path. Anat. 29; 423, 1918-1919 | ♂ R | | | Yes; 4 days after incision for suppurating lymph glands | <p>October, 1916, patient was taken with pain in right side of neck and dysphagia; February, 1917, right side of neck began to swell; April 6, 1917, diagnosed abscess and incised; only on escape of thick stream of blood did operator realize nature of malady; gauze tampons used to still hemorrhage; necropsy: aneurysm of internal carotid artery just above its origin; soft tissues bathed with purulent secretion</p> |

which was in turn succeeded by an energetically pulsating lump. The mass collapsed on compression of the common carotid artery and on puncture furnished pure blood. Though the patient received no treatment, the swelling diminished to the vanishing point in three months. Ligation of the internal carotid artery was considered but rejected on account of the poor condition of the patient.

The most striking feature in this group of cases is the extreme youthfulness of the patients, twelve being recorded as under 21 years of age. This is a matter of no little practical significance, as peritonsillar abscess is a very common disease in young people. That treatment appropriate to the latter may lead to grave consequences if applied to the former is strikingly attested by the death of four of these patients. Wulff was spared this embarrassment by ligating the common carotid artery, but Liston, Vas, Velebil and Schlagenhauser were not so fortunate. Helman under similar circumstances changed the diagnosis of a colleague from abscess to aneurysm. This patient was later operated on at another clinic, but died of a postoperative pneumonia. Zamboni saw a case that others had diagnosed as abscess and advised incision. He recognized the nature of the affection, ligated the internal carotid artery and saved the patient's life. On the other hand, the proclivity of this aneurysm to spontaneous rupture has led to equally disastrous consequences by the physician in charge failing to recognize its nature. A case in point is that of Neuffer. The patient had had an angina tonsillaris, followed by an increasing enlargement of the left tonsil. As the disease progressed the food passage became so narrowed as to prevent the swallowing of solids and the jaws could be opened only a slight distance. On the twelfth day of the disease the patient had a profuse hemorrhage from the mouth with a fatal repetition the next day. The source of the hemorrhage remained in doubt until necropsy revealed an aneurysm of the internal carotid with an opening into the mouth. Among others Johnson lost a patient under quite similar circumstances. In view of the catastrophes mentioned in the foregoing the prompt recognition of faucal aneurysm consecutive to scarlet fever, influenza, cervical adenitis, septic sore throat and inflammatory tonsillar disease is of the utmost importance, as a false move may jeopardize the safety of the patient's life.

In addition to the cases tabulated, Molinié¹⁵ cites the following suggestive case. The patient, a woman, who had suffered with an otitis media from infancy, underwent an operation in 1898, evidently for mastoiditis. In 1905, a second operation was interrupted by the occurrence of a profuse hemorrhage, which was controlled by packing the

15. Molinié: *Rev. de laryngol., d'otol et de rhinol.* **13**:97, 1921; abstr. by Bourgeois: *J. de chir.* **18**:254, 1921.

wound with gauze. Ultimately the cavity filled up with a dark red tumor from which, without apparent reason, two hemorrhages occurred. The lump pulsated neither to sight nor to touch unless compressed when an indistinct pulsation was both seen and felt. In 1906, paralysis of the facial nerve developed and in 1920, of the auditory, the glossopharyngeal, the pneumogastric and the spinal accessory. Molinié at first regarded the lesion as an arterial or an arteriovenous aneurysm, but later discarded this diagnosis in favor of dilatation of the lateral sinus and bulb of the internal jugular vein, ascribing the pulsation to transmission of the cerebral pulse. Another doubtful case is that reported by Majewski.¹⁶

The patient, a man, aged 64, complained of a pain in his neck of three weeks' duration, and for two weeks he had had a swelling in the left side of the neck. The overlying skin was neither raised nor red. The lump was opened under ethyl chlorid applied locally, and a small amount of whitish exudate was evacuated. Eight days later blood escaped from the wound. This was arrested by tampons. On the eleventh day during the process of redressing there was a repetition of the bleeding. Again tampons staunched the flow of blood. Three days later there was a renewal of the bleeding. This time the flow could not be stopped by pressure, so the patient was taken into the hospital, where an incision was made through the previous operative site. The hemorrhage was now found to be deep seated. First, the internal carotid artery was tied near its origin, but as the bleeding continued, the vessel was still further exposed and a rent from which the blood was pouring was disclosed. A second ligature was placed above this point. The bleeding now stopped, but the day following there was some elevation of temperature, a pulse rate of 120, and a fully developed hemiplegia. Death occurred thirty-six hours after the operation. Helman¹⁷ refers to two cases of large vascular pharyngeal enlargements reported by Stoerck¹⁸ as hematomas from which when opened a profuse hemorrhage flowed, the arrest of which proved exceedingly difficult. From the description Helman says that it is extremely difficult to judge whether these were aneurysms or inflammatory swellings with bloody contents. This author also mentions that in 1895 Grossmann showed a case of aneurysm of the throat successfully treated by ligation of the common carotid artery before the Vienna Laryngologic Society. Schulte¹⁹ reports the following case:

A woman, aged 26, consulted him, Oct. 8, 1903, for a running from the ear which she had had off and on for many years. On examination Schulte discovered a superficially smooth, bluish red growth which he took for a polypus

16. Majewski: *Kron. lek.* 24:658, 1903.

17. Helman: *Medycyna i. Kron. lek.* 44:685, 1909.

18. Stoerck: *Nothnagel's Special Pathology* 13.

19. Schulte: *Monatschr. f. Ohrenh.* 38:117, 1904.

projecting through a rent in the ear drum. He incised this and was rewarded with the escape of a strong stream of bright red blood. The flow was brought partially under control by gauze packs and the diagnosis changed to aneurysm of the internal carotid artery. As from time to time there was a renewal of the bleeding, Dr. Schneider made a ligation of the common carotid artery, October 11, apparently with success; but the next day the bleeding recurred and did so daily until October 15, when a solution of gelatin was injected into the patient. There was no further bleeding until October 26, then a daily repetition to October 30, and from then to November 18, intermittently, when following a total of nineteen injections of gelatin, the hemorrhage finally ceased. The patient was discharged, December 14, as cured.

Hirsch²⁰ states that Heine found an aneurysm of the internal carotid artery in a 53 year old man. Concerning the further course of the case he could add nothing. This is in all probability the same case that Heine²¹ reports under the title of bleeding from the internal carotid artery in consequence of erosion.

A woman, aged 56, was admitted to the hospital, Feb. 13, 1900. At 3 years of age she noticed a swelling behind the right ear. This opened at the age of 6 and discharged for fifteen years. Pain was first felt in August, 1899, and some days later a right hemicrania developed. At the base of the right mastoid process was a fistula filled with a bad smelling mass. February 16, a radical mastoidectomy was done and the patient was discharged April 14, with the wound still running. She was readmitted August 27, and the wound was curetted the same day. During the maneuvers the carotid artery was exposed. To the sight it did not pulsate. At the change of dressings, September 1, a stream of dark blood suddenly escaped. Pressure on the common carotid did not influence the flow. Arrest of the hemorrhage was finally accomplished by iodoform gauze tampons. He attributed the hemorrhage to an erosion of the internal jugular vein. The bleeding recurred several times thereafter, but was easily controlled by pressure. The woman, however, did badly and died, October 1. Necropsy showed that the blood had come from an erosion of the internal carotid artery superinduced by middle ear disease, and death was caused by sepsis.

Benjamins²² records a case of aneurysm of the right internal carotid artery with fatal bleeding from the external auditory meatus from necrosis of the floor of the canal following the insufflation of powdered arsenic for the cure of a discharge. The patient, a woman, fell into Benjamins' hands shortly after, but died. Necropsy revealed an aneurysm of the internal carotid, but I could not determine whether it was in the extracranial portion of the vessel or in the bony canal. Certainly there were no pharyngeal symptoms. At the time of the hemorrhage Benjamins believed the source of the bleeding an eroded

20. Hirsch: *Monatschr. f. Ohrenh. u. Laryngo-Rhinol.* 48:782, 1914.

21. Heine: *Berl. klin. Wchnschr.* 38:619, 1901.

22. Benjamins: *Arch. f. Ohrenh.* 76:240, 1908.

jugular vein because pressure on the common carotid artery failed to stop the hemorrhage. Quite a similar case is that of Ruttin.²³

A soldier was admitted to the hospital, Jan. 17, 1918, for bleeding from the left ear, nose and mouth. In November, 1917, while serving on the Italian front, he was buried by the explosion of a shell. Since 1914, he had had a discharging left ear which was rendered worse by the accident. On entrance the left ear was discharging a quantity of foul pus and the patient complained of severe pain in the head. After admission the hemorrhage from the nose, mouth and ear renewed itself on several occasions. Jan. 18, 1918, a radical mastoid operation was undertaken. January 20, there was renewed bleeding from the mouth and nose, and the man died. Necropsy showed the presence of an aneurysm of the internal carotid artery in the knee of the carotid canal, the wall of which was eroded.

Ehrmann²⁴ of Mulhouse reports the following suggestive case:

A man, aged 22, entered the hospital, April 28, 1875, in the service of Dr. Battenburg, for an angina tonsillaris of a few days' duration which had localized on the right side. He complained of pain in the right submaxillary region, dysphagia and fever. May 1, the abscess opened spontaneously into the throat, at which time a stream of red blood flooded the mouth. This ceased spontaneously, but a few hours later a new hemorrhage occurred. It was as sudden in onset as the first, but less abundant. Inspection of the throat, which was accomplished with difficulty owing to the locking of the jaws, revealed redness, edema and tumefaction of the velum, and a distinct impulse was imparted to a palpating finger. Soon there was a repetition of the bleeding but on a grander scale. The patient was now in a state of syncope, quite exsanguinated with a thready pulse and cold extremities. Delay was no longer permissible, so Ehrmann, with the assistance of Battenburg, made a ligation of the common carotid artery. On account of the size of the swelling the vessel had to be ligated below the omohyoid muscle. The postoperative course was favorable. At no time were there any cerebral or nervous symptoms. The patient was discharged cured, June 18, 1875. Ehrmann considered this a case of erosion on the internal carotid artery.

TRAUMATIC TYPE

A striking feature of this series is the relatively large number of aneurysms of this vessel reported as following gunshot wounds incurred either in the Balkan or the World Wars. As a result of these struggles fourteen case reports have found their way into print, whereas so far as I could determine the internal carotid artery had escaped this lesion in previous wars. This immunity has been explained by the blunter shape of the bullets in former days and the slower speed at which they traveled. On the other hand, most of the cases occurring in civil practice have been the result of knife or puncture wounds. No matter how produced, traumatic aneurysm of the internal carotid artery has the same

23. Ruttin: *Beitr. z. Anat., Physiol., Path. u. Therap. d. Ohres* 11:224, 1919.

24. Ehrmann: *Bull. et mém. Soc. de chir. de Paris* 55:664, 1878.

practical interest to the surgeon and the physician as the types already discussed, for like them it has on occasion been mistaken for abscess and has been lanced, with unfortunate results. Of no less importance is the tendency of this aneurysm if left untreated to rupture spontaneously with the premature death of the patient. Of the treated patients a fair proportion are saved; in the untreated, an exceedingly high mortality rate is to be expected.

The patients numbered twenty-seven, of which thirteen, or 48.15 per cent., recovered; thirteen, or 48.15 per cent., died, and one, or 3.7 per cent., was discharged unimproved. Twenty-five were males; one was a female. In one the sex was not mentioned. The ages ranged between 6 and 37 years, respectively, thirteen being 17 years or over, two less than 17; in nine cases the patients were described as soldiers and in one as a sailor. Presumably, the latter were young adults. In one no clue to the age was given. A noticeable feature of this series is the comparative youth of the victims. As one would naturally suppose from males being more exposed to injury, the men far outnumber the women, being in the proportion 25:1. Twenty-one were operated on, with thirteen, or 61.91 per cent., cures; and eight, or 38.09 per cent., deaths (Table 9). Six patients were not operated on, with five, or 83.33 per cent., deaths; the other, Orth's patient, refused operation, passed from under his care and was presumably lost sight of as no mention was made of the ultimate outcome (Table 10). The right side was affected fifteen times; the left, six. In six instances the side on which the lesion was located was not mentioned. The aneurysm was attributed to puncture wound once; to stab wound, four times; to pistol or bullet wound, nine times; to missile wound, once; to shell splinter, twice; to severe injury received two years before in a bicycle collision, once. The cause of seven was not mentioned. Six of the latter were soldiers, and the probability is that in these the primary injury was a gunshot wound. The deaths in the operative cases were assigned to cerebral softening three times; to sepsis, once; to softening of the brain and pneumonia, once; to the closing of wound on operating table, once; to secondary hemorrhage, once. The nonoperative deaths were attributed to spontaneous hemorrhage twice; to uncontrollable hemorrhage when aneurysm was mistaken for abscess and lanced, once; to thrombosis of vertebral artery, once; to softening of the brain, once.

The vessels ligated and the results were as follows: common carotid artery, nine times, with four cures and five deaths; common and internal carotid arteries, above and below sac, with opening of the sac, once, with cure; common, external and internal carotid arteries and superior thyroid artery, extirpation of sac, once, with cure; common carotid artery and internal jugular vein, once, with cure; common carotid and internal

carotid arteries, once, with cure; common carotid artery, incision and packing of sac, twice, with two cures; common carotid, later external and internal carotid arteries, once, with cure; internal carotid artery, twice, with one recovery and one death; internal carotid artery, above and below sac, extirpation of sac, once, with death; internal carotid artery, suture of proximal segment and double ligation of internal jugular vein, once, with cure; internal carotid artery, above sac, common carotid, below, and internal jugular vein, once, with cure.

Lee fifteen days after the accident noticed a swelling in the hard and soft palate which he mistook for an abscess; he lanced it and was surprised with a gush of bright red arterial blood, accompanied by a peculiar noise. All attempts to stem the flow were prevented by the struggles of the patient, who died in a few minutes. Booth's patient was seen by a number of physicians, most of whom were inclined to the diagnosis of peritonsillar abscess. There never was any apparent pulsation in the lesion, which was hard and firm to touch. A profuse, spontaneous hemorrhage proved fatal in a few minutes.

The story of traumatic aneurysm in the cervical portion of the internal carotid artery would be incomplete were the following cases passed by in silence. The reports themselves will indicate the reason for their deletion. The nature of the case reported by Matas,²⁵ and cited as a possible example of extracranial aneurysm of the internal carotid artery, is no longer in doubt. March 11, 1924, Matas²⁶ said:

I notice that you refer to my early case of suspected aneurysm of the internal carotid artery. In this case the death of the patient about a year after my report cleared all doubt. The patient returned with a decided increase in the tumor with secondary growths in the corresponding cervical glands. After preliminary tracheotomy, I made an attempt to extirpate the mass, which projected into the pharynx. The patient survived the operation only a few weeks. The tumor proved to be a fibrosarcoma. There is no question that in this case there was no aneurysm, though the clinical history and symptomatology simulated an aneurysm so closely that there was always a doubt as to the true nature of the tumor until the final outcome proved unequivocally that it was not. However, you will agree that in the case that I reported Logan and Souchon had good reasons for their diagnosis.

It is only fair to Matas to state that from the beginning he believed the case a fibro-adenoma of the tonsil, but his colleagues, Logan and Souchon, were as firmly convinced as to its aneurysmal nature. As most of the mistakes in diagnosis have been in the opposite direction the history of this case is worthy of relating. The patient, a man, aged 35, had had an inflammation of the throat simulating an abscess six years before. This was punctured by a local physician, but without result.

25. Matas, Rudolph: *New Orleans M. & S. J.* 22:245, 1894-1895.

26. Matas, Rudolph: Personal communication to author.

TABLE 9.—*Traumatic Aneurysms Operated On*

| Case | Author and Reference | Sex; Age; Side | Duration | Operation Date | Cured | Died; Cause | Remarks |
|------|--|----------------|----------|--|-------|--|---|
| 1 | Mattucci: <i>Ann. J. M. Sc.</i> 18:551, 1869 | ♂ 25 R | 6 weeks | Ligation common carotid artery, 3/8/1862 | | Yes, 12 days after operation; softening of right hemisphere | Puncture wound; day after operation paralyzed in left leg and arm; gradually grew worse until death; necropsy |
| 2 | Baker: <i>Nashville J. Med. & Surg.</i> 7:402, 1871 | ♂ 23 L | 6 weeks | Ligation common and internal carotid arteries, 2/23/1871 | Yes | | Stub wound, middle of January, 1871; admitted, February 8, for a circumscribed, smooth, strongly pulsating, expansile swelling in left parotid region; bruited; lump in throat; dysphagia; volume lessened by pressure to common carotid artery; compression used to no avail, the mass enlarging daily; patient alive and well in 1880 |
| 3 | Prewitt: <i>Tr. Ann. S. A.</i> 4:233, 1886 | ♀ 17 R | 4 months | Ligation common carotid artery; tube drainage, 4/4/1885 | | Yes, 25 days after operation; thrombosis right lateral and inferior petrosal sinuses | Bullet wound in married negro; increasing pharyngeal swelling, pulsating in every direction; thrill; bruited; projecting externally behind jaw; paralysis of pharyngeal muscles; loss of taste right half of tongue; pain in head and neck; headache; roaring in right ear; muffled voice; dysphagia; pulsation controlled by compressing common carotid; 8 days after operation bleeding from external wall of sac; repeated following days, so sac was incised and its cavity packed with gauze; bleeding arrested; convulsions on the twenty-third day, repeated until death; necropsy; bullet found in sac |
| 4 | Duchamp: <i>L'ovre méd.</i> 17: 113, 1891 | ♂ 32 R | 8 days | Ligation common carotid artery, 8/27/1891; ligation external and internal carotid arteries, 9/5/1891 | Yes | | Admitted, Aug. 20, 1891, for a pistol wound; there was slight swelling but no pulsation; at end of 8 days, swelling had taken on appearance of an abscess, but pulsation was discernible to both sight and touch and was arrested by pressure on common carotid, which indicated clearly its nature; situation was dangerous, especially as patient had had several slight hemorrhages from mouth; with tying of knot pulsation ceased immediately, to return 3 days later, rendering a second intervention imperative; after completion of latter operation, patient's mouth was opened to view result; there was spurt of blood from orifice of bullet; a finger was inserted into rent until it could be plugged with gauze; no further bleeding occurred; patient was alive 7 years later |
| 5 | Ciechowski: <i>In Lewenstein: Gaz. lek.</i> 21:658, 1901 | ♂ 29 R | 1 day | Ligation common carotid artery, 8/20/1897 | Yes | | Cut with knife in August, 1897, following day at site of injury an increasing hematoma appeared which interfered with speech; 14 days later patient admitted to hospital, for an expansile swelling in parotid region, evident to both sight and touch, hard and painful and of such volume as to cause disfigurement; slight thrill present; muscles supplied by facial, hypoglossal and recurrent laryngeal nerves paralyzed; pulsation arrested by compressing common carotid; right tonsil was pushed inward to midline, red and swollen; mass soft, pulsating and expansile; dysphagia; spoke in a whisper; diagnosis: aneurysm internal carotid; with tying of ligature, all motion in mass ceased; swelling gradually subsided; swallowing became possible and voice returned; 3 years later patient was in good health; no evidence of the aneurysm |
| 6 | Robbio: <i>Pollendico, chir.</i> 13:50, 1903 | ♂ 20 L | 1 day | Ligation common carotid artery, 3/8/1904 | Yes | | Knife wound, left side of neck, Jan. 18, 1901; almost complete loss of voice; large subcutaneous cervicofacial hemorrhage; laryngeal stenosis; voice husky, almost aphonic; dyspnea; paralysis left vocal cord and left side of tongue; tonsil pushed inward to median line by bulging of pharyngeal wall; February 24, patient felt pulsation in submaxillary region; bimanual examination showed fluctuating and compressible tumor; on compression of carotid, pulsation disappeared and mass was noticeably diminished in volume; with ligation pulsation ceased; when discharged there was no detectable pulsation, but nervous phenomena persisted |

| | | | | | | |
|----|---|------------|--|------|--|---|
| 7 | Gilbert; Arch. f. Klin. Chir. 108: 557, 1916 | | Ligation internal carotid artery, about 12/3 | | Yes, in 4 days; softening of brain and pneumonia | Article is lacking in details; patient was Serbian soldier wounded in Balkan War, 1912-1915; immediately after operation patient lost consciousness; then pneumonia developed; necropsy |
| 8 | Stearns; Bull. et Arch. Chir. 127: 460, 1916 | 5 months | Ligation internal carotid artery and extirpation of sac, 5/9/1915 | | Yes, in 56 hours; hemiplegia from embolus | Soldier, wounded by bullet in battle, June 25, 1914; on admission pulsating tumor high up in left side of neck; integument thin but intact; pulsation expansile; mass slightly reducible on pressure; bruit; paralysis of left sternocleidomastoid and trapezius muscles, left half of tongue and left vocal cord; no immediate signs of intracranial mischief on day following; epileptiform seizure and right hemiplegia; condition gradually grew worse until death; no necropsy |
| 9 | Paget, in Makins; Brit. J. Surg. 3: 212, 1915 | 5 days | Ligation common carotid artery | Yes | | Missile injury received in World War; patient presented tense swelling of soft palate, which gradually faded away after ligation; tying of artery caused no cerebral symptoms; there was a right facial weakness |
| 10 | Hochstedt; Rev. f. Chir. de Strasbourg, 30: 304, 1916 | 15 days | Ligation common carotid artery, 6/6/1915 | Yes | | Soldier received pistol wound in 1915; apparently making smooth recovery when, June 6, he had a severe hemorrhage from wound; at no time were there any cerebral symptoms |
| 11 | Kobinger; Tschech. Jb., 58: 1041, 1916 | | Ligation common, external, internal carotids, superior thyroid arteries and internal jugular vein, with extirpation of the sac, 7/3/1916 | Yes | | A soldier was admitted, June 23, 1916, for a shell wound in upper right cervical region, where there was diffuse swelling; July 21, was convalescing nicely |
| 12 | Polbram; Arch. f. Klin. Chir. 108: 650, 1917 | | Ligation internal carotid artery | | Yes, on third day; cerebral softening | Paralysis appeared on side opposite wound day following operation; necropsy |
| 13 | Polbram; Arch. f. Klin. Chir. 108: 650, 1917 | 1 month | Ligation internal carotid artery, 12/11/1916 | Yes | | Turkish soldier wounded by shell splinter, Oct. 14, 1916; right sided paralysis of facial, glossopharyngeal and hypoglossal nerves; severe pain in ear and neck; pulsating swelling with systolic blow; dysphagia; pharyngeal swelling size of walnut; it had all appearances of retropharyngeal abscess; during succeeding days symptoms became more aggravated and with pulsation and thrill led to diagnosis of aneurysm of internal carotid; at no time was there pain or cerebral disturbances; 2 months after operation he was quite well, and paralysis had disappeared |
| 14 | Polbram; Arch. f. Klin. Chir. 108: 650, 1917 | | Ligation common carotid artery | | Yes, in 10 days; cerebral softening | After ligation patient did nicely for 4 days, then flaccid paralysis supervened in leg and arm of side opposite injury; necropsy |
| 15 | Gilbert; Pollehnico. med. prat. 25: 557, 1916 | Short time | Ligation internal and common carotid arteries and internal jugular vein, 6/20/1917 | Yes | | Shrapnel wound received June 20, 1917; right side of neck seat of tumor, size of apple; dysphagia, hoarseness; dyspnea; cyanosis; lump soft and compressible and pulsated synchronously with opposite carotid; mass pulsatile throughout; paralysis of right side of soft palate, of tongue and of right vocal cord; sac found at operation to arise from internal carotid just above bifurcation; at end of 2 months paralysis had disappeared with exception of slight deviation of tongue to right |
| 16 | Rauchschleber; Arch. f. Klin. Chir. 110: 700, 1916 | 2 weeks | Suture of proximal segment of internal carotid artery and ligation internal jugular vein, 11/6/1916 | | Yes, on table while wound was being closed | Wounded, Sept. 29, 1916; no swelling in neck or throat, no pulsation, no bruit; movements of jaw unimpeded; speech indistinct; incomplete paralysis of left upper extremity, complete of left lower; October 25, wound in neck suppurated, reopened and drained; October 31, spontaneous hemorrhage, cause a purpura; temperature now septic and jaws locked; November 5, small, tender, pulpy area showed in neck; November 6, bruit detectable; diagnosis made at operation; vessel had been completely severed; necropsy revealed organizing clot in cerebral end of internal carotid and softening of brain |

TABLE 9.—*Traumatic Aneurysms Operated On—(Continued)*

| Case | Author and Reference | Sex; Age; Side | Duration | Operation Date | Cured | Died; Cause | Remarks |
|------|---|----------------|----------|---|-------|---|---|
| 17 | Sanders; J. Roy. M. Ser-vice 51101, 1919 | ♂ Man R | 1 week | Ligation common carotid artery. 6/25/1917 | | Yes, in 14 days; hemorrhage from rupture of sac | Bullet wound, right side of neck, June 13, 1917, causing hematoma; fifth day pulsation noticed and thought to be expansile, and soft systolic blow audible; soon aneurysm definitely increasing in size; patient's condition daily becoming worse; 4 days after operation some return of pulsation; on fourteenth day lower end of sac burst into wound; although bleeding was promptly stemmed, patient died in 2½ hours; necropsy: internal carotid severed at its origin; no supuration in wound |
| 18 | Vegas; Rev. espan. de med y cirug. 31:251, 1920 | ♂ do L | 1 year | Ligation common carotid artery and internal jugular vein, 4/16/1917 | Yes | | Admitted, March 18, 1917, for pulsating lump in left side of neck consecutive to pistol wound; size of hen's egg, pulsated synchronously with radial artery and expanded throughout; bruit; slight thrill; diagnosis: aneurysm of internal carotid; March 18, right hemiplegia appeared, which was attributed to embolus; though patient had experienced paralytic stroke, indented vessels were ligated; April 30 tumor had almost disappeared and paralysis was slowly improving |
| 19 | Cauvel; Riforma 30:417, 1920 | .. | 1 month | Ligation common carotid artery, incision and packing of aneurysmal cavity | Yes | | Knife wound; no cerebral symptoms; paper was presented before Societa Medico-Chirurgica Anconitana, Jan. 30, 1920; source given here was only an abstract and supplied no details of case |
| 20 | Official History of the Great War Medical Services, Surgery of the War, London, 1922, 2:243 | ♂ Soldier | | Ligation common and internal carotid arteries | Yes | | Hemorrhage from leaking aneurysm connected with commencement of internal carotid; no complications following operation |
| 21 | Camera; Minerva med. 22:720, 1922 | ♂ do R | 1 month | Ligation common carotid artery; then accidental opening of sac during attempted enucleation, enlargement of opening, extrusion of coagulum, free bright red hemorrhage controlled by packing, 4/23/1922 | Yes | | Pistol wound received March 19, 1922, ball entering just below infra-orbital margin and lodging in upper part of right sternocleidomastoid muscle; patient first seen by Camera, April 19, 1922, for diffuse tumefaction of right cervical region situated in front of ear and extending from thyroid cartilage below to angle of jaw above; overlying skin thinned, and behind sternomastoid was open wound made 10 days after accident for purpose of extracting bullet which had been localized by roentgen ray; on admission patient looked ill; was dyspneic; could open mouth only 1.5 cm.; saliva drooled constantly; voice was husky; tongue when protruded, deviated to right and angle of mouth pulled to left; there was great displacement of right lateral pharyngeal wall which reached quite to median line; mass elastic in consistency; fluctuated; was slightly painful; harbored neither beads nor bruits; intra-oral palpation could not be made on account of inability of patient to open mouth; interference with swallowing; exploratory puncture had given exit to bright red blood; clinical impression was aneurysm in extracranial portion of internal carotid artery; postoperative course was uneventful and the patient was discharged as cured, May 25, 1922; at that time hypoglossal and vagal paralyses persisted; facial paresis was somewhat improved; patient was swallowing food without difficulty and pharyngeal swelling had receded to its normal limits |

TABLE 10.—*Traumatic Aneurysms Not Operated On*

| Case | Author and Reference | Sex, Age, Side | Duration | Cured | Died; Cause | Remarks |
|------|---|-------------------|-----------|------------|---|--|
| 22 | Ferguson: <i>Trans. Med. Zeitung</i> 74: 18, 1904 | ♂ 37 R | 9 months | | Yes; hemorrhage; spontaneous rupture | Puncture of throat by stem of pipe; 5 days later pain in throat and stiffness of right side of neck; examination revealed pulsation in right parotid region and red and swollen palate; swelling remained stationary for 8 months, then commenced to increase in size; finally hemorrhage from mouth which stopped spontaneously. to be followed 6 hours later by fatal bleeding; necropsy revealed aneurysm of internal carotid artery and close by missing piece of pipe stem |
| 23 | Lutz, in <i>Fraenkel and Leq. Gall. Med.</i> 3: 375 10, 1902 | ♂ 22 R | 15 days | | Yes, immediately; incised for abscess, with mortal hemorrhage | Bullet wound; subsequent swelling in right parotid region; 15 days later swelling of hard and soft palates had appeared; aphonia, dysphagia and pain in right side of neck; with considerable difficulty patient succeeded in opening mouth sufficiently to permit limited inspection; tonsil and soft palate much swollen and on hard palate was small, firm tumor about size of hickory nut; thinking this the ball, Lutz made incision; there was gush of blood which could not be brought under control; necropsy by Fenker revealed aneurysm of internal carotid artery |
| 24 | Booth: <i>Philadelphia M. J.</i> 61: 100, 1900 | ♂ 25 L | 18 days | | Yes, in 10 days; hemorrhage | Trouble began Jan. 1, 1900; diagnosed as chronic quinsy, complicated by hemorrhage; when first seen by Booth, January 8, there was a mass in left tonsillar region extending to fauces; section from growth showed no signs of malignancy; never any apparent pulsation in lesion, which was hard and firm to touch; January 29, profuse hemorrhage, which proved fatal in few minutes; Booth considered case traumatic aneurysm consecutive to severe injury received two years before in bicycle collision while coasting; necropsy: aneurysm of internal carotid |
| 25 | Bull, in <i>Kocher's Beitr. z. Klin. Chir.</i> 108: 16, 43, 1907 | ♂ 31 R | | | Yes, March 13, 1905; thrombosis of the circle of Willis, right and left internal carotids, etc. | Soldier wounded, Oct. 5, 1904, by gunshot projectile; tender swelling in left side of neck; roaring in ear; pulsation; no thrill; slight systolic bruit; March 12, 1905, hier ligated left common carotid artery just below sac; as further freeing of primitive carotid failed to demonstrate the aneurysm as arising from it, he incised the sac and pulse retained hemorrhage by introduction of finger; breathing suddenly ceased, but pulse retained good tone; after tracheotomy, breathing was reestablished, but patient failed to rally; necropsy: aneurysm of left vertebral artery, but what is of more interest, a penetrating wound of right internal carotid artery, on each side of which was aneurysm size of hazelnut and filled with firm clot |
| 26 | Orth: <i>Beitr. z. Klin. Chir.</i> 105: 367, 1907 | ♂ Soldier L | Some time | Unimproved | | Headache; neuralgia in neck and left side of head; patient could not be induced to undergo operation; further details wanting |
| 27 | Johnson, in <i>Gabriel's Beitr. z. Klin. Chir.</i> 110: 183, 1909 | ♂ Soldier | 1 month | | Yes; softening of brain | Wounded, July 2, 1918; Diagnosis, aneurysm of external carotid; August 23, vessel exposed, with failure to locate lesion; external carotid artery ligated, however; patient died same evening; necropsy revealed aneurysm of internal carotid artery and softening of brain |

Examination revealed an intrabuccal and extrabuccal lump that pulsated strongly. The patient complained of dysphagia and his life was threatened by suffocation. An aneurysm of the right internal carotid artery was suspected, possibly of traumatic origin, and the corresponding common carotid artery was ligated at the point of election. The lump decreased in size but was persistent for two years. It did not pulsate. The man was improved in health. In view of the confusing nature of this case, its final disposition is a matter of no little interest.

An undoubtedly genuine case of traumatic aneurysm of the internal carotid artery, operated on by Bossowski and reported by Helman,²⁷ must be excluded from my list as neither the original article nor a transcript was accessible to me. Helman merely mentions the case without supplying any of the details. Rauchenbichler²⁸ describes a case that he clinically diagnosed as an aneurysm of the internal or of the common carotid artery. A man, aged 57, wounded himself with a knifelike instrument in the left side of the neck eight days before examination. The ensuing hemorrhage, which was free, was controlled by suture of the soft parts and a firm bandage. From the moment of the injury there was speech disturbance, but no other paralysis. Eight days after the accident, a swelling developed at the site of the wound. It was at this time that the patient was brought to the hospital. In the left side of the neck, corresponding to the course of the great vessels, was a fluctuating, expansile swelling the size of a hen's egg, with a systolic blow. The pulsation was influenced greatly by compression of the common carotid, but not completely arrested. Other than the statement that the author intended later to perform arteriorrhaphy no details are furnished concerning the case. The vessel at fault therefore remains in doubt.

Frisch²⁹ presented before the Royal Society of Physicians of Vienna, at the Dec. 10, 1915 meeting, a patient with what he believed an aneurysm of the internal carotid artery located in the neck close to the base of the skull. The trouble originated from a gunshot wound. The presence of such signs as hoarseness, atrophy of the sternocleidomastoid muscle, shrinkage of the half of the tongue corresponding to the injured side, the development of a contracted pupil and ptosis on the side of the injury indicated damage to the vagus, spinal accessory, hypoglossal and cervical sympathetic nerves. Behind the angle of the

27. Helman: *Medycyna i. Kron. lek.* 44:708, 1909.

28. Rauchenbichler: *Wien. klin. Wchnschr.* 26:84, 1913.

29. Frisch: *Berl. klin. Wchnschr.* 53:99, 1916.

jaw was a pulsating swelling. Calcium lactate administered by mouth and pressure applied directly to the mass caused the pulsations to become less pronounced. While this is probably an aneurysm of the vessel under discussion, the evidence is not such as to warrant its inclusion in the tables.

Gasne³⁰ reports quite a similar case. A soldier was injured, March 12, 1916, by the concussion of a shell, as evidenced by the absence of a wound and failure to find, by roentgen-ray examinations, any foreign body embedded in the tissues. There was bleeding from the left ear, hemicrania, aphonia, embarrassed respiration and a tumefaction in the left carotid region. When admitted to the hospital, March 21, the entire left carotid and parotid regions were markedly tumefied. To touch, the involved area felt doughy rather than fluctuating, and exhibited neither expansion nor pulsation. Behind the angle of the jaw was a genuine tumor as large as an apricot, round, limited and animated by expansion and beats, and the seat of a soufflé. Examination of the pharynx was difficult, owing to the pain produced by opening the mouth. The entire left wall of the pharynx was bulging. Gradually the swelling diminished, but the aneurysm preserved its characteristic features until April 6, when it began to fade away. By April 23, there were no more beats or soufflé, and the swelling had almost entirely disappeared. The man was discharged, May 31, 1916. Six months later he was again at the front. Though ignorant of the patient's future course, Gasne regarded the swelling as an example of rupture of a large vessel from the shock of a bursting shell, which terminated in a spontaneous cure. He thought the vessel involved one of the carotids.

Knaggs³¹ says that during the World War he had to deal with only four aneurysms of the neck. One of these arose from the neighborhood of the bifurcation, but unfortunately the writer does not mention which vessel was involved, and the description is such as to leave the reader in doubt. A soldier was wounded, Dec. 12, 1916. When he came under observation, December 27, there was a pulsating swelling, the size of a chestnut, behind the angle of the left jaw. It felt like a mass of inflammatory tissue. Jan. 26, 1917, a short, sharp systolic murmur appeared and the pulsation became expansile. The external carotid felt thicker at its most superficial part when compared with that on the other side, and the main swelling blended with this thickened part.

30. Gasne: *Paris chirurg.* 12:212, 1920.

31. Knaggs, R. L.: *Brit. J. Surg.* 8:167 (Oct.) 1920.

Jan. 27, 1917, the left common carotid artery was exposed and a temporary ligature applied at the level of the cricoid cartilage. A dissection of the sac was made, and its whole anterior surface and sides were exposed. It extended from the level of the bifurcation to the posterior belly of the digastric muscle. The parts were so matted as to render impossible the recognition of the anatomic structures involved or to complete the removal of the sac without danger of injury to important structures; consequently, the operation was concluded by tying the common carotid, without seeking the fragment of metal to which the lesion was attributed. May 14, the swelling had completely disappeared, its site being indicated by a little thickening. There was no bruit and the lesion appeared completely cured.

Goldamer³² reports the case of a soldier who had a tear at the point where the right internal and external arteries diverge, the aneurysm being formed at the expense of both vessels. The wound in the external carotid was treated by lateral suture. The internal carotid was too badly damaged for restorative purposes and required a ligation. For many days after the operation the patient lay in a stupor with his eyes turned to the side of the injury and with spastic paralysis of the opposite side of the body. These serious symptoms developed despite a week's preliminary compression of the common carotid. The man finally regained complete health. It is mentioned that Reich³³ exhibited a man with simultaneous aneurysms of the internal and external carotid arteries due to gunshot wound at the Dec. 2, 1914 session of the Medizinische-Naturwissenschaftlicher Verein Tuebingen. However, no details are furnished. Herzen³⁴ saw an aneurysm involving both the internal and the external carotids simultaneously in a soldier wounded in the Russo-Japanese War, and in another soldier, one of the internal carotid artery. These cases are simply mentioned, no data being furnished.

The case is mentioned of a soldier who had had all three carotid arteries ligated for an aneurysm at the bifurcation. No other information is given except that the patient made a good recovery, without any impairment of power.

The cases of von Eiselsberg and Matthews, though not so stated, are apparently of the intracranial type. The case observed by von Eiselsberg

32. Goldamer: *Beitr. z. klin. Chir.* **106**:605, 1917.

33. Reich: *München. med. Wchnschr.* **62**:200, 1915.

34. Herzen: *Chirurgia* **30**:95, 1911; *abstr. J. de chir.* **7**:677, 1911.

was reported by Ranzi.³⁵ A soldier, aged 26, was admitted into the hospital, Feb. 17, 1917, for a wound received in the left cheek, fracture of the mandibular ramus, ankylosis of the jaw, exophthalmos, edema of the eyelid and a distinct roaring in the neighborhood of the parietal bone. Pinching of the exposed external carotid did not influence the noise, but with occlusion of the internal branch, the roaring was controlled. Therefore, April 12, the lumen of the left internal carotid was occluded to about three-fourths its normal caliber. October 26, one-half a year after the operation, the exophthalmos was reported as substantially improved and the noise greatly diminished. Matthews³⁶ records a case of somewhat the same character. A man was kicked by a horse on the left side of the head just above the zygoma, July 22, 1905. About a week afterward he developed a squint in the left eye. In September, 1905, he noticed impairment of vision. Somewhat later a buzzing sound appeared, with its point of greatest intensity located in the region of the zygoma. There was no external swelling, no pulsation, but a well marked bruit could be heard over the pterygoid region and the upper part of the posterior triangle. This could be stopped by compression of the common carotid artery. June 30, 1906, the common carotid artery was tied. The patient made an excellent recovery. Both the bruit and the buzzing entirely disappeared.

ARTERIOVENOUS TYPE

Aneurysms of the arteriovenous type number nineteen, of which eighteen were males and one a female. The ages of twelve only were recorded. The youngest was 20 and the eldest 48 years old. Nine were in their twenties; two, in their thirties, and one was in his forties. Seven were described as soldiers and two as men. All the cases resulted from trauma. Nine times the aneurysm was caused by bullets; four times by shrapnel; once by a stab wound; four times by war injuries; once from the concussion of a bursting shell, and twice by trauma. It is notably a disease of young male adults. Up to 1914, only four writers described this lesion; viz., Joret (1840), Giralès (1854), Keen (1894) and Janssen (1903). Of the fifteen remaining patients thirteen were soldiers wounded in battle during the World War. Sixteen were operated on, with fifteen cures, or 93.75 per cent., and one failure, or 6.25 per cent. (Table 11). Three were treated expectantly, with 100 per cent. mortality; one died of cerebral softening and epilepsy thirty hours after the receipt of the injury; one succumbed from anthrax

35. Ranzi: *Arch. f. klin. Chir.* **110**:656, 1918.

36. Matthews: *J. Roy. M. Corps*, London **8**:1437, 1907.

TABLE 11.—*Arteriovenous Aneurysms Operated On*

| Case | Author and Reference | Sex; Age; Side | Duration | Operation Date | Cured | Died; Cause | Remarks |
|------|---|----------------|---------------|---|-----------------------------|-------------|--|
| 1 | Reu. Med. A. Surg. Rep. Porter, Philadelphia, 7015-9, 1934 | ♂ 25 L | 2 years | Ligation common carotid, external carotid and internal jugular vein, 8/15/1933 | Yes | | Bullet wound; when first seen, Aug. 9, 1933, had contractures of right arm; aneurysmal bruit, thrill in left side of neck; slight external swelling; sought relief for persistent noise in ear, which prevented him from working; after operation, no mental disturbances; slight ptosis; pupils not affected, responded to light |
| 2 | Janacek; Ein Fall v. Aneur. aneurism der Carotidis interna u. Vena jugularis communis sinistra infolge Stielverletzung. Kiel, 1902, p. 11 | ♂ 21 L | 1 day | Ligation common carotid, external carotid, internal carotid, superior thyroid arteries and internal jugular vein, 8/22/1902 | Yes | | Stab wound; first seen, Aug. 21, 1902, with pulsating swelling behind angle of left jaw; it was elastic and had thrill and souffle; condition considered dangerous; no untoward symptoms after ligation, save a persistent inequality of pupils |
| 3 | Haberer; Wien. klin. Wochenschr. 27:1477, 1914; also Arch. f. klin. Chir. 107:625, 1910 | ♂ 34 R | About 5 weeks | Quadruple ligation and extirpation of sac, 1914 | Yes | | Soldier, wounded, Aug. 28, 1914; weakness in left extremities; dizziness; headache; behind angle of right jaw whirring swelling; paralysis of right sympathetic nerve; damage to right vagus nerve; after operation headache was relieved and paralysis gradually cleared up; Oct. 28, 1914, considered cured |
| 4 | Gilson-Hermans; J. belge de chir., 14:71, 1914, quoted by Leuermant, J. de chir. 17:133, 1921 | ♂ Soldier | | Ligation common, external and internal carotid arteries and internal jugular vein | Yes | | Bullet wound; 2 months later appearance of pulsation and thrill without tumor |
| 5 | Hand-Sutton; Brit. J. Surg. 3:469, 1915 | ♀ 27 L | 7 weeks | Quadruple ligation, 12/5/1914 | Yes | | Bullet wound, accidental; swelling; loud buzzing in left ear; thrill; murmur; operation followed by paralysis of right leg and arm; diplopia; hemorrhagic papillitis and double optic neuritis; complications attributed to thrombosis of cavernous sinus |
| 6 | Bier; Deutsch. med. Wochenschr. 41:122; 123, 1915 | ♂ Soldier | | Vessel suture, 1914 | Yes | | Article contains no definite description of case; author states that during short space of 2 months, terminating Dec. 1, 1914, he had operated on 44 aneurysms in 43 patients; patient was disturbed both night and day by roaring in head; he mentions he had seen similar case in consultation |
| 7 | Lannols and Patel; Canad. J. Surg. 15:127, 1915; also, Patel; Lyon chir. 20:311, 1923 | ♂ 22 R | 8 months | Ligation common carotid artery and internal jugular vein, obliteration of right lateral sinus by tamponade, 4/22/1915 | No recurrence | | Soldier, wounded by bullet, Aug. 26, 1914; symptoms: auditory disturbances; thrill; bruit; right lingual and laryngeal paralysis; immediate results were excellent, but on reexamination 7½ years afterward aneurysm had reformed; Patel withheld further operation for fear of result on cerebral circulation |
| 8 | Dufourmentel; Presse med. 25:160, 1917 | ♂ 23 L | 8 months | Ligation internal sinus, 10/25/1915; ligation internal carotid artery, 11/10/1915 | Yes, after second operation | | Soldier, bullet wound, Feb. 28, 1915; Oct. 5, 1915, while undergoing examination for deafness, purple, violently pulsating tumor noticed in floor of left external auditory canal; with first stroke of curet, profuse hemorrhage, controlled by tamponade; October 25, internal carotid artery exposed; as pressure on this vessel did not entirely control bleeding, under supposition that it came from internal jugular vein, rapid trephinement was made, left lateral sinus being laid bare and ligated; as bleeding repeated itself at each dressing, souffle persisted and pulsating tumor remained in floor of canal, internal carotid was again isolated and ligated, without the least immediate or remote cerebral disturbance |
| 9 | Ostenberg; München. med. Wochenschr. 64:237, 1917 | ♂ 24 L | | Ligation vertebral, internal and common carotid arteries, sac incised and packed with gauze, 11/1/1916 | Yes | | Shell wound, with aneurysm of internal carotid artery, vertebral artery and lateral sinus; had had operation for cervical swelling believed to be an abscess; as free hemorrhage occurred, wound was closed and firm compression exerted; on entrance, powerfully pulsating swelling in left side of neck; first common and internal carotid arteries exposed and loose ligatures thrown around them; next, subclavian artery uncovered, vertebral located and tied; pulsation now weaker but not entirely stilled until internal carotid was ligated; believing circulation in sac controlled, it was laid wide open; immediate copious hemorrhage, arrested with the tightening of ligature around common carotid artery; clots removed and shell fragment extracted; occipital bone fractured and lateral sinus torn; tamponade of sac, wound partially closed; for a time loss of use of right leg, attributed to area of softening in left hemisphere |

| | | | | | | | |
|----|---|-------------------|----------------|---|----------|-------|---|
| 10 | LaFort: Bull. Acad. de Méd. 78: 108, 1917 | ♂ Man L | 3 months | Ligation internal jugular vein above and below fistula, sac incised, artery sutured, suture line reinforced by wall of vein | Yes | | Bullet wound; thrill in left side of neck; arrested by pressure; thumping in head; symptoms increasing in severity; with temporary ligatures removed, circulation through carotids was restored; after operation, no nervous phenomena |
| 11 | Soubeyran: Rev. gén. de clin. et de thérap. 31: 376, 1917 | ♂ Soldier L | | Ligation common and external carotid arteries, ligation of sac, tamponade, 5/12/1917 | Yes | | Bullet wound; diffuse left parotid swelling, activated by neither beats nor souffle; blood withdrawn on aspiration; first external carotid artery ligated and sac split, but as blood continued to trickle, common carotid was tied and sac packed; no facial paralysis |
| 12 | Suchanek: Arch. f. klin. Chir. 110: 682, 1918 | ♂ Soldier R | About 6 months | Ligation of internal jugular vein near base of skull, narrowing internal carotid with muscled sling from sternocleidomastoid; 6 days later, ligation internal carotid artery proximally | Yes | | Gunshot wound; spastic paralysis left side of body; roaring in right ear; loud bruit over internal jugular vein, disappeared on compressing vein above; first operation under local anesthesia 25 weeks after injury, caused roaring in ear to disappear, but aneurysm reformed; pulsation became ever palmer, overlying soft structures thinner and thinner; rupture threatened and second operation was undertaken; paralysis improving when patient was discharged; in spite of existing hemiplegia, which induced employment of less radical method, no distressing symptoms were observed when circulation was totally cut off |
| 13 | Gault: XXXI Cong. franç. d'oto-rhinolaryng., quoted by Lenormant, J. de chir. 17: 188, 1921 | ♂ Soldier | | Ligation internal jugular vein below the lesion, tamponading lateral sinus through a mastoid trephinement; ligation, next day, common carotid artery | Yes | | Shell wound; profuse secondary hemorrhage from pharynx; intrapharyngeal compression; then operation |
| 14 | Official History of the Great War, Medical Services, Surgery of the Vessels, London, 2: 243, 1922 | ♂ Soldier | | Ligation common carotid artery | Improved | | No cerebral disturbance followed but actual result on aneurysm was doubtful |
| 15 | Official History of the Great War, Medical Services, Surgery of the Vessels, London, 2: 237, 1922 | ♂ Soldier | 6 weeks | Suture vent in vein, plication of sac | Improved | | Shrapnel wound; left sympathetic paralysis; 6 weeks later aneurysm was explored; sac was found interposed between internal jugular vein and lower end of internal carotid artery; when control ligatures had been tightened, sac was opened, but free hemorrhage accentuated clamping ascending pharyngeal and superior thyroid arteries; postoperatively some thickening at site of sac and hoarse, systolic bruit, but both were steadily improving |
| 16 | Rouviellois: Bull. Acad. de Méd. 91: 705, 1924 | ♂ 22 R | 4 days | Ligation common, external and internal carotid arteries and internal jugular vein, with extirpation of sac, 9/5/1916 | Yes | | Soldier, thrown violently to ground by concussion of bursting shell without leaving slightest trace of wound; vertigo; deafness; severe pain in right side of neck; on examination, tumefaction which beat in harmony with pulse behind angle of right jaw; thrill; souffle; slight nonpulsatile bulging right tonsillar region to sight, but to touch animated by beats; moderate exophthalmos, unassociated with pupillary or motor disturbances; slight dysphagia; slightly husky voice; paralysis of right vocal cord; no respiratory embarrassment, roentgenogram negative; postoperative course satisfactory; immediate and gratifying relief from humming in ear and annoying souffle, which had prevented all sleep; June 8, 1924, patient in good health |

forty-four days after the accident, and one expired about three weeks after the receipt of the trauma (Table 12). A noteworthy feature of the operative series was the multiplicity of methods employed, with about equal success.

The methods were: ligation of the common carotid and the external carotid arteries and the internal jugular vein, one case; ligation of the common, external and internal carotid arteries and the internal jugular vein, two cases; ligation of the common carotid artery and internal jugular vein, with obliteration of the right lateral sinus by tamponade, one case; ligation of the common carotid, the internal carotid and the vertebral arteries, incision of the sac, gauze packing, one case; ligation of the common and external carotid arteries, splitting of the sac, packing, one case; ligation of the common carotid artery, one case; ligation of the common carotid artery and the internal jugular vein below the lesion, tamponading of the lateral sinus through an opening in the mastoid, one case; quadruple ligation, one case; quadruple ligation, extirpation of the sac, one case; ligation of internal carotid artery and lateral sinus, one case; ligation of common, external and internal carotid arteries and the internal jugular vein, with extirpation of the sac, one case; ligation and division of the internal jugular vein at the base of the skull, first narrowing of internal carotid artery by muscle sling, later proximal ligation, one case; suture of vent in vein, plication of sac over hole in the artery, one case; suture of vessel, no data given, one case; ligation of the internal jugular vein above and below the lesion, arteriorrhaphy and capping with the sac wall, one case.

In view of the wide range of operations employed, the results are truly remarkable. The sole failure was the observation of Lannois and Patel³⁷ published as a success, following a tamponading of the right lateral sinus and ligation of the common carotid artery and the internal jugular vein. The immediate results were excellent. The objective and subjective phenomena disappeared promptly and the man was returned to active service. However, on reexamination 7½ years later, Patel³⁸ reports that the man had in the meanwhile developed a diffuse tumefaction of the right half of the face which resembled a large angioma, marked dilatation of the veins at the angle of the jaw and large pulsating venous lakes in the submaxillary region, with a systolic blow. The blood pressure, 25 systolic and 150 diastolic, indicated a leakage in the arterial system. Despite the application of three

37. Lannois and Patel: *Caducée* 15:127, 1915.

38. Patel: *Lyon chirurg.* 20:341, 1923.

ligatures, two venous and one arterial, to the common carotid artery just below its bifurcation, the external carotid artery had permitted the reestablishment of the intracranial circulation and at the same time pumped blood into all the branches of the internal jugular vein between the ligatures. Patel contented himself by remarking that ligation of the external carotid artery and the peripheral venous branches should lessen the vascular phenomena, but would not be without danger to the cerebral circulation. Leriche advised operation in spite of the technical difficulties on account of the rapidly developing cardiopathy in this type of case. Berard, in discussing the observation mentioned above, reported a case of arteriovenous aneurysm that he saw in 1916 at Paris; this case involved the internal jugular vein and the external and internal carotid arteries near their origin, and was at first treated by ligation of the common carotid artery and the internal jugular vein. The operation afforded some months of amelioration, when suddenly, following an effort, the signs of the arteriovenous aneurysm recurred. The condition was relieved by extirpation of the sac and ligation of all the contributory vessels.

In view of the fact that these aneurysms are liable to recur after a simple ligation of the vessels at fault, it would appear the better policy, whenever possible, to extirpate the sac by some such plan as practiced by Haberer and afterward by Rouvillois, unless a restorative operation is feasible; the latter course is preferable on account of the lessened chances of interference with the cerebral circulation. After restorative aneurysmorrhaphy, however, the possible formation of an arterial aneurysm must be considered. There are none in this group, but Reid³⁹ reports such a complication in an arteriovenous aneurysm of the right femoral vessels.

The question has arisen as to the most propitious time to operate, early or late. Lavenant⁴⁰ favors delayed operation in the belief that this plan jeopardizes life the least; but he says that an operation that restores the current in the artery is better still.

Almost invariably this lesion is caused by penetrating foreign bodies, such as bullets, pieces of shell and knives. The case of Rouvillois is a notable exception. After a most careful search of the literature I could find only one case of a like nature. This was reported by Gasne.⁴¹

39. Reid, M. R.: Abnormal Arteriovenous Communications, Acquired and Congenital, *Arch. Surg.* **10**:601 (March) 1925, Case 10.

40. Lavenant: *Paris chirurg.* **11**:369, 1919.

41. Gasne: *Paris chirurg.* **12**:212, 1920.

TABLE 12.—*Arteriovenous Aneurysms Not Operated On*

| Case | Author and Reference | Sex; Age; Side | Duration | Cured | Died; Cause | Remarks |
|------|---|----------------|---------------|-------|---------------------------------------|---|
| 17 | Jorat: <i>Gaz. méd. de Paris</i> 8: 457, 1840 | ♂ 35 L | 30 months | | Yes; cerebral softening and epilepsy | Bullet wound, May 2, 1835; died, Oct. 23, 1837; four months after injury, epileptiform seizures and tumor size of pigeon's egg in left side of neck, with thrill and pulsation apparent to both patient and physician; necropsy: ball found encapsulated in internal jugular vein |
| 18 | Giraldès: <i>Bull. Soc. de chir. de Paris</i> 5: 70, 1854 | ♂ Man L | 1 month | | Yes, in 44 days; anthrax | Bullet wound, June 16, 1854; swelling, thrill and murmur; necropsy: ball found in sac joining artery to vein |
| 19 | De Ruffele: <i>Riforma med.</i> 36: 345, 1920 | ♂ 20 R | About 3 weeks | | Yes, Sept. 30, 1916; abscess of brain | Soldier, wounded, July 11, 1916; weakly pulsating swelling in parotidæan region; on palpation, elastic, expansile throughout; thrill; systolic blow on auscultation; on compression of common carotid souffle became weaker; small, oval, soft tumefaction in right pharyngeal wall, which bulged into and slightly constricted alimentary tract; ptosis of right lid, weakness right facial muscles, interference with speech, annoying noises in right ear; dyspnea; dangerous cerebral symptoms when primitive carotid artery was compressed discouraged surgery; necropsy: aneurysm about 4 cm. above bifurcation |

A soldier was injured, March 12, 1916, by the concussion of a shell, as evidenced by the absence of a wound and failure to find, by roentgen-ray examination, any foreign body embedded in the tissues. There was bleeding from the left ear, hemicrania, aphonia, embarrassed respiration and a tumefaction in the left carotid region. When the patient was admitted to the hospital, March 21, the entire left parotid and carotid regions were noticeably swollen. The involved area felt doughy rather than fluctuating, and exhibited neither expansion nor pulsation. Behind the angle of the jaw was a mass as large as an apricot, round, limited, animated by expansile beats, and the seat of a distinct souffle. Examination of the pharynx was difficult owing to the pain produced by opening the mouth. Gradually the swelling diminished. However, the aneurysm preserved its characteristic features until April 6, when it began to fade away. By April 23, there were no more beats or bruit and the swelling had almost entirely disappeared. The man was discharged, May 31, 1916. Six months later he was again at the front. Gasne regarded the swelling as an example of a rupture of a large vessel from the shock of a bursting shell which terminated in a spontaneous cure. He thought the vessel involved was one of the carotids.

Leconte and Oury⁴² have described what they believe to be an analogous observation, but of the common carotid artery. The most remarkable feature of their case is the length of time that had elapsed between the receipt of the injury and the appearance of the vascular disease. In addition the case is another example of dilatation of the right ventricle, rather than of the left, following arteriovenous fistulas in the several regions of the body. A man, aged 31, was seen by Laubry, May 9, 1924, for dyspnea and distressing buzzing in the left side of the face. In 1917 he had received a bullet wound in the right cervical region. According to his statement, the wound was superficial and the projectile was easily extracted. Cicatrization occupied only a few days. It was further learned that the man at the time of the injury had suffered a severe concussion and had lost consciousness. From 1917 to 1922 he had led an absolutely normal life. In 1922, after any effort he began to experience some shortness of breath. For two years this was practically the only symptom. It was at first transitory, but finally led him to discontinue all work. More recently he had had attacks of vertigo, and on one occasion a syncope of short duration. Some weeks before this time another symptom appeared, an annoying sensation in the left cervical region, associated with an intermittent buzzing in the left ear and

42. Leconte and Oury: *Bull. et mém. Soc. méd. d. hôp. de Paris* 48:906, 1924.

rhythmic pulsations in the head. Examination of the precordial and the left cervical regions left no doubt as to the cause of the trouble. In close proximity to the left sternoclavicular articulation, the examiner felt an intense thrill, heard a loud murmur of systolic intensification, and perceived a decidedly abnormal bulging in the course of the cervical vessels, with arterial expansion. Fluoroscopy disclosed a decided bulging in both the right chambers of the heart. An electrocardiogram, however, did not show anything abnormal in the tracings. A Wassermann test was negative, as was the remainder of the examination. Although the only hope for relief held out to the patient was operation, he refused to avail himself of the chance thus offered. A somewhat similar case has been reported by Ruttin.⁴³ A soldier was admitted to the hospital, Jan. 17, 1918, for bleeding from the left ear, the nose and the mouth. In November, 1917, while serving on the Italian front, he was buried by the explosion of a shell. Since 1914 he had had a discharging left ear, which was rendered worse by the accident. On entrance the left ear was discharging a quantity of foul pus and the patient complained of severe pain in the head. After admission the hemorrhage from the nose, the mouth and the ear renewed itself on several occasions; therefore, on Jan. 18, 1918, a radical mastoid operation was undertaken. January 20, there was renewed bleeding from the mouth and the nose, and the man died. Necropsy showed the presence of an aneurysm of the internal carotid artery in the knee of the carotid canal, the wall of which was eroded. As will be noticed, the cases of Heuer and Cushing have not been included in the present tables. Though my authority, Callander,⁴⁴ did not specifically say that they were extracranial, I interpreted them in my earlier paper as such, but wrongfully as these cases are classed as intracranial in an article by Reid.⁴⁵ A revision is therefore necessary, and they must be dropped as examples of the lesion under discussion.

In conclusion I cannot impress on the profession too forcibly that aneurysm of the internal carotid artery in its cervical portion is not the rare lesion that it once was thought to be; that it is not a benign lesion, as the many catastrophes related in this study bear witness; that operative attack offers a fair percentage of cures, while pacific management or internal therapeusis is almost invariably followed by death. While spontaneous cure may occur, it is unusual, only one instance in this series

43. Ruttin: *Beitr. z. Anat., Physiol., Path. u. Therap. d. Ohres* 11:224, 1919.

44. Callander: *Johns Hopkins Hos. Rep.* 19:301-302, 1921.

45. Reid (Footnote 39, Cases 5 and 11).

being so recorded. A sufficient number of observations have been placed on record to serve as a warning to physicians that a unilateral lump in the throat may be an aneurysm and should be so regarded until proved otherwise, if unfortunate disasters are to be avoided. It is far better to be careful than to be sorry afterward and to repent at leisure a hasty act.⁴⁶

46. Since this article was written the following example of spontaneous aneurysm in the extracranial portion of the internal carotid artery has been published by Reid (Aneurysms in the Johns Hopkins Hospital, *Arch. Surg.* 12:1-74 [Jan.] 1924, Case 55). The patient, a white woman, aged 61, married, was admitted to the hospital, Aug. 27, 1919, for an extracranial aneurysm of the right internal carotid artery of one year's duration. She gave no history of syphilis and the Wassermann reaction was negative. The trouble began with a tickling sensation in the throat. Later, a swelling resembling a peritonsillar abscess protruded into the right side of the pharynx. Eight weeks before admission an incision had been made into this swelling. The mass was pulsatile and involved the soft palate and tonsil. It did not show externally. September 2, Reid ligated the right internal carotid artery. Occlusion of the external carotid artery had no effect on the aneurysm. The pulsation (much reduced by the operation) promptly returned and lasted for eight days. During this time there was an intense right sided headache. Then the aneurysm clotted, pulsation stopped and the headache had become much less before her discharge. At no time were there any signs of paralysis. May 29, 1922, the patient wrote that she still felt a little fulness in the throat, which, however, did not pulsate.

THE FUNDAMENTAL PRINCIPLES OF THE TREATMENT OF GASTRIC AND DUODENAL ULCERS*

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The final decision as to the choice of a surgical procedure for the cure of gastric and duodenal ulcers must rest at present on the empirical observations of our statistical studies. That operation is best which gives the best results in the largest number of cases and which can be performed with a low mortality. Such a purely empirical attitude is forced on us by our lack of knowledge both of the normal and the pathologic physiology of the stomach and of the etiology of the lesion we attempt to treat. But at the same time this method, though necessary at present, is not the ideal scientific attitude, which seeks rather to base its procedures on demonstrable truths. The numerous studies, on man and the lower animals, striving steadily to establish those facts which will permit us rationally to conceive and carry out our surgical procedures are slowly beginning to bear fruit. The first step of a scientific inquiry is the accumulation of facts. The second is the attempt to establish some principles that will explain these facts. Perhaps we are already justified in attempting the latter. This article will discuss some of these fundamental principles that have already been accepted by many and at the same time point out what they permit us to explain and what they portend for the future surgical therapeutics of gastric and duodenal ulcers.

PREDISPOSITION TO ULCER

There is an individual predisposition to gastric and duodenal ulcers. There has long been a feeling among physicians and surgeons that most patients with gastric and duodenal ulcers belong to a definite group. This belief is the result of observations of numerous points of similarity among these patients and of the marked tendency in them of the ulcer to recur. The question is, of course, part of the much larger problem of congenital diathesis and acquired predisposition to disease. The pursuit of such an inquiry is manifestly beset with many difficulties. In the first place, a workable and inclusive classification is necessary to permit the charting of the similarities and differences among men.

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Draper¹ has suggested the following classification. He calls his divisions the "panels of personality," and labels them under the separate headings (1) anatomy, (2) physiology, (3) psychology and (4) immunity. If we accept this classification, we may say that the work that has been done along these lines to ascertain the characteristics of the "ulcer group" may, with the exception of Draper's anatomic studies, be included under the heading physiology. The physiologic observations follow.

Von Bergman's² Views.—In chronic lead poisoning the structures of the nervous system are markedly affected. The destructive lesions, however, are found not only in the peripheral nervous system and brain but also in the vegetative nervous system. Thus degeneration of the vagus may occur. Further, a large number of patients suffering from this malady present symptoms markedly resembling those of peptic ulcer. And in the statistics that he quotes one third of these were definitely proved to be due to ulcer. We have, then, an appreciable number of patients developing a gastric ulcer following (1) a destructive lesion of the autonomic nervous system, and (2) a tendency to colic, that is, muscular spasm.

Von Bergman then argues by analogy that other causes may bring about a disharmony between the vagus and the splanchnic systems, and similarly produce localized or generalized spasms in the muscles of the stomach or duodenum, or in the terminal blood vessels. Persons suffering from ulcer often possess a large number of disturbances in the autonomic nervous system, but we cannot accurately classify them, for the symptom complexes of disorders within this system have not as yet been precisely defined. The further elaboration of his theory into the actual causation of the ulcer by digestion of the ischemic area need not be considered here. What concerns us now is his contention that in a large number of patients with ulcer definite variations from the normal are found in the autonomic nervous system. These variations have further been carefully studied by Westphall.³ To the argument that many patients with these changes do not develop ulcer, von Bergman counters that the ulcer is merely a local manifestation of a systemic condition. In the same way not every patient suffering from syphilis develops tabes. The latter condition is merely an occasional local manifestation.

1. Draper, G.: Diagnosis and Treatment, *Endocrinology* 3:164 (April-June) 1919.

2. Von Bergman, G.: Zur Pathogenese des chronischen Ulcus pepticum, *Berl. klin. Wchnschr.* 55:524, 1918.

3. Westphall, K.: Untersuchungen zur Frage der nervösen Entstehung peptische Ulcera, *Deutsches Arch. f. klin. Med.* 114:327, 1914.

Hurst's⁴ Views.—The examinations of normal students⁵ show that in some there is a persistent hypertonic stomach associated with hyperchlorhydria. These, he says, have “an inborn variation from the average normal, which manifests itself in hypertonus of the stomach with active peristalsis, rapid evacuation, and hyperchlorhydria with hypersecretion.” This is caused “no doubt by an unusual degree of tonic activity of the vagus nucleus; it is strictly localized to that part which controls the activities of the stomach, and is not accompanied by a slow pulse or other signs of general vagotonia.” This diathesis may be retained throughout life without the development of a pathologic lesion. But because of the greater peristaltic activity of these stomachs there is swept over into the duodenal cap larger quantities of a more concentrated acid, especially during the intervals between meals when the normal stomach usually is at rest. The actual cause of the ulcer he believes to be a bacterial infection, but the more or less constant presence of acid in the duodenal bulb is a contributing cause for its persistence. He has not encountered a case of duodenal ulcer except in a patient with this type of stomach, and he believes further that this “hypersthenic gastric diathesis” persists after the ulcer heals spontaneously, or even after gastro-enterostomy. Hurst, like von Bergman, emphasizes a basic change in the autonomic nervous system, but interprets its effects in a different way.

Koennecke,⁶ while studying the effects of the pylorus on the genesis of ulcer, performed some experiments that bear on this problem. He sidetracked the antrum and pylorus and established a direct continuity between the body of the stomach and the duodenum. This was without appreciable effect. If in addition to these procedures the splanchnic nerves were divided in the abdomen, and the branches of the celiac ganglions also were severed then in a large percentage of cases ulcers developed. Here we have the experimental production of what might be termed an abdominal vagotonia, or at any rate a disturbance in the normal workings of the autonomic nervous system. It seems possible that this may have produced the disposition to ulcer, and that other factors, later to be discussed, were directly responsible.

4. Hurst, A. F.: The Hypersthenic Gastric Diathesis, *Lancet* 2:1369 (Dec. 30) 1922; Pathogenesis of Gastric and Duodenal Ulcer, *Guy's Hosp. Rep.* 74:413 (Oct.) 1924.

5. Baird, M. M.; Campbell, J. M. H., and Hern, J. R. B.: The Importance of Estimating Chlorides in the Fractional Test Meal Samples, and Some Experiments with the Duodenal Tube, *Guy's Hosp. Rep.* 74:23 (Jan.) 1924. Campbell, J. M. H., and Conybeare, J. J.: Comparison of the Test Meal and X-Ray Examination of the Stomach in Health, *Guy's Hosp. Rep.* 74:354 (July) 1924.

6. Koennecke, W.: Experimentelle Untersuchungen über die Bedeutung des Pylorusmagens für die Ulcusgenese, *Arch. f. klin. Chir.* 120:537, 1922.

In their anthropometric studies, Dunn and Seegal⁷ found that patients with peptic ulcer presented definite anatomic variations when compared with those suffering from gallstones. These differences were remarkably constant.

Mention was made above of Draper's classification of men for the investigation of individual variations; namely, (1) anatomy, (2) physiology, (3) psychology and (4) immunity. It does not seem likely (although we cannot say with certainty) that any studies to prove individual predisposition to ulcer could be performed under the third heading, that is, psychology. But if, as Rosenau maintains, a streptococcus that possesses an elective affinity for the stomach and first part of the duodenum is the immediate cause of ulcer, it would appear that fruitful results might be achieved by investigations under the fourth heading, that is, immunity.

Concerning the first postulate, that there is an individual predisposition to ulcer, we may say in conclusion that it is not as yet proved; that, however, even the foregoing brief survey shows adequate grounds for its acceptance as a working hypothesis, and that it yields the possibility of numerous further suppositions whose investigation should be of distinct value.

THE RELATION OF HYDROCHLORIC ACID TO ULCER

Hydrochloric acid is an essential factor in the production of ulcer. A little reflection on the pathogenesis of gastric and duodenal ulcers soon forces on us the conviction that hydrochloric acid is in some way intimately bound up with their production. These ulcers occur where acid occurs. Under normal conditions this means in the stomach and beginning of the duodenum. But when a new passage is created between the stomach and some other portion of the intestinal tract and acid reaches these strange parts, then ulcers may promptly appear. Gastrojejunal or jejunal ulcers are only too well known. And recently Berg⁸ found a large indurated gastro-ileal ulcer in a patient where a surgeon had by mistake performed a gastro-ileostomy.

Of course, the argument that some ulcers are found when the test meals shows an anacidity immediately comes to mind. This objection will be fully answered presently.

Before we consider in detail the relation of acid to ulcer it will be necessary to consider the changes that have taken place in our conception of the regulation of gastric acidity. An understanding of this mechanism is also essential for an evaluation of the various surgical procedures.

7. Draper, G. D.; Dunn, H. L., and Seegal, D.: Studies in Human Constitution: 1, Clinical Anthropometry, J. A. M. A. 82:431 (Feb. 9) 1924.

8. Berg, A. A.: Personal communication to the author.

*Mechanism of the Pylorus.*⁹—Material of fluid or pulpy consistency is forced into the antrum by the tonus of the fundus and body and by the peristaltic waves of the latter. Every advancing peristaltic wave in the antrum normally forces a portion of this chyme into the duodenum. The remainder slips backward through the circular opening of the advancing wave. During the early part of digestion if a solid piece of food finds its way into the antrum, it is carried back to the body by retrograde peristalsis. During the latter part of digestion the consistency of the expressed material seems to be thicker. In other words, it is the *fluidity* of the gastric contents that is of prime importance. The acidity on the gastric or duodenal side of the pylorus does not control the opening and closure of that sphincter during digestion.

Following the entrance of food into the stomach the pylorus attains a certain degree of tone. This tone may result in its closure, but it yields readily to an increase of pressure in the antrum produced by contractions of the latter. Normally, during the greater part of the progress of the peristaltic wave through the antrum, the pressure is sufficiently high to force fluid chyme in a steady stream through the diaphragm-like opening of the pylorus, regardless of the reaction of this chyme. When the peristaltic wave reaches the pylorus it then effects a firm closure of this sphincter and prevents regurgitation of the material that has just been forced through. When four waves per minute are coursing over the stomach the length of time during which the pylorus is open and chyme is being forced through averages about ten or eleven seconds. The length of time which the sphincter is closed after the wave has reached it averages from about four to five seconds. In other words the pylorus is open for a greater length of time than it is closed. I am speaking now, of course, of the period of digestion, and when peristaltic waves are passing down the stomach. Furthermore, retrograde peristalsis in the duodenum may force back intestinal fluids through the pylorus at any time that the pressure there is higher than that in the antrum.

The important things to remember are that during digestion (1) the pylorus is open more of the time than it is closed, and (2) mere pressure relations govern the to-and-fro passage of fluids through this sphincter.

Regulation of Gastric Acidity.—Pure gastric juice as it is secreted by the stomach contains from 0.35 to 0.5 per cent hydrochloric acid. The researches of Pawlow¹⁰ established this and innumerable observations by

9. For a complete consideration of the experiments leading to the following conclusions the reader is referred to Klein, E.: *Gastric Motility: III. The Mechanism of the Pylorus*, Arch. Surg. 12:1224 (July) 1926.

10. Pawlow, I. P.: *The Work of the Digestive Glands*, translated by W. H. Thompson, London, 1910.

others have since confirmed it. This corresponds to a free hydrochloric acid of from 95 to 135. On the other hand, the acidity of the gastric contents at the height of digestion usually does not go higher than 0.2 per cent. What accounts for the difference? At first thought one would attribute it to the dilution accomplished by the food. However, the intestinal tract cannot only reduce the strength of its own acidity, but if 0.5 per cent hydrochloric acid is introduced by mouth or through a gastric fistula, there is a progressive reduction effected in the concentration, and the motility is markedly delayed until this occurs. Boldyreff¹¹ first showed that this reduction is accomplished by a regurgitation of the alkaline pancreatic juice. By successively excluding all possible factors, such as the bile, the intestinal juice, the saliva and an alkaline secretion from the stomach, he found that none of these could bring about an appreciable reduction. Only the pancreatic juice was very potent, and if it was excluded the concentration of acidity remained almost unchanged.

Boldyreff's conclusions are being more widely accepted every day.¹² Among some of those who agree may be mentioned Hicks and Visser, Spencer, Neyer, Rehfuess and Hawk, Deutsch and Rürup, Morse, Gross¹³ and others.

Bolton and Goodhart¹⁴ have recently also added evidence from test meal observations. In the tabulation of the results of the Rehfuess test meal there is in the majority of normal cases a rather rapid rise of the concentration of hydrochloric acid till the maximum is reached in about one and one-half hours. From this peak there is a sharp decline. They found by chloride determinations that this sudden diminution in the concentration of hydrochloric acid was not due to dilution, but to a neutralization. And further observation convinced them that the alkali of the pancreatic juice was responsible.

11. Boldyreff: The Self Regulation of the Acidity of the Gastric Contents and the Real Acidity of the Gastric Juice, *Quart. J. Exper. Physiol.* 8:1, 1914.

12. For a complete discussion the reader is referred to Klein (Footnote 9).

13. Hicks and Visser: The Mechanism of the Regurgitation of Duodenal Contents into the Stomach, *Am. J. Physiol.* 39:1, 1915. Spencer, W. H.; Meyer, G. P.; Rehfuess, M. E., and Hawk, P. B.: Direct Evidence of Duodenal Regurgitation and Its Influence upon the Chemistry and Function of the Normal Human Stomach, *Am. J. Physiol.* 39:459 (Feb.) 1916. Deutsch, G., and Rürup, H.: Ueber den Rückfluss von Pankreassaft in den Magen und die Bestimmung der Salzsäurerestenz des Trypsins, *Deutsches Arch. f. klin. Med.* 138:165 (Jan.) 1922. Morse, W. E.: The Relation of Acid to Gastric Discharge and Duodenal Regurgitation in the Dog, *Am. J. Physiol.* 41:439 (Oct.) 1916. Gross, O.: Ueber der physiologischer Rückfluss von Pankreassaft in den Magen, *Deutsches Arch. f. klin. Med.* 132:121 (April) 1920.

14. Bolton, C., and Goodhart, G. W.: Duodenal Regurgitation into the Stomach During Gastric Digestion, *Lancet* 1:420 (March 4) 1922.

We have then a nice mechanism that, when the acid concentration in the stomach reaches a certain level, normally accomplishes its reduction. The regurgitation probably follows on the stimulation of the duodenal mucosa by irritant concentrations of acid.¹⁵

As a result of these observations we must now divide all cases of anacidity into two groups. In the first no acid is secreted and an examination of the total chlorides in the gastric test meal will show that they are low. In the second group, there may be no free acid but the total chlorides are high. As these chlorides come almost entirely from hydrochloric acid, this means that the acid *was* secreted but was subsequently neutralized. Thus Bennett and Ryle¹⁶ had come to the conclusion from examination of normal medical students that about 4 per cent of people have achlorhydria. Baird, Campbell and Hearn later performed similar test meals, again on medical students, and at the same time made chloride determinations. They encountered four cases of anacidity. Three of these were shown to be due to neutralization of hydrochloric acid that had been secreted. The fourth was a true achlorhydria and was in an individual who was not healthy.

Hyperchlorhydria is due to faulty neutralization. Granted that intestinal regurgitation is the mechanism for the reduction of acidity, then every case of hyperchlorhydria is in the last analysis due to faulty neutralization. It is, of course, remembered that acid is secreted at a concentration of from 0.35 to 0.5 per cent, or in the language of the test meal from 95 to 135 free hydrochloric acid. This faulty neutralization may be due to either (1) chemical or (2) mechanical factors.

(1) It is conceivable that if there is too much acid, as in hypersecretion, the normal amount of alkali will be insufficient to neutralize it. On the other hand there may under exceptional conditions be an insufficient quantity of alkali available.⁵ I do not believe either of these factors to be often responsible for marked variations from the normal in gastric acidity.

(2) I believe that the mechanical or pressure relations more often are at fault. Too great pressure on the gastric side may prevent adequate regurgitation of the pancreatic juice. This may occur, for instance, in the hypertonic stomach, so strongly emphasized by Hurst,⁴ or with hyperstalsis. But the fault may also lie on the duodenal side. I do not know of anyone who has mentioned this, but it may be of great importance, especially in pathologic states. We do not know definitely the manner in which the duodenum forces back contents into the stomach.

15. Klein (footnote 9).

16. Bennett, T. I., and Ryle, J. A.: A Study of Normal Gastric Function Based on the Investigation of One Hundred Healthy Men by Means of the Fractional Method of Gastric Analysis, *Guy's Hosp. Rep.* 71:286 (July) 1921.

Presumably it is by retrograde peristalsis, for that type of muscular activity is known to occur there. It is reasonable to suppose that the nervous mechanism which is responsible for this peristalsis may be deranged because of a pathologic lesion, such as an ulcer, or that the actual destruction of muscular tissue and the adhesions resulting from an ulcer may directly interfere with the peristaltic waves and the creation of sufficient pressure to force the duodenal contents back into the stomach. That marked deformities of the duodenum often result is well known. This is again recently emphasized by Robertson and Hargis.¹⁷

The pylorospasm or organic obstruction that often accompanies ulcer is a further hindrance to proper neutralization. Very high acidities are usually encountered in cases of pyloric stenosis. I believe that these mechanical interferences with the normal pressure relations are by far the most common cause of hyperchlorhydria.

Experimental Influence of Acid on Ulcers.—We may now briefly¹⁸ review some of the experimental work relating to the influence of acid on ulcer. This work has been in part along two lines, first, the addition of large quantities of acid to the gastric contents, and, second, the elimination of the normal alkaline juices, thus indirectly increasing the acidity. One should nevertheless not lose sight of the probability that it is not necessarily increased acidity as is so often demanded but rather merely acidity which is necessary for the pathogenesis of ulcer in the predisposed human being.

In one type of experiment¹⁹ the duodenum was extirpated and the pancreatic juice was either deflected to the surface or to a lower portion of the gastro-intestinal tract. The result was that a highly acid gastric juice entered the jejunum and ulcers were frequently found to follow. If the acid was again neutralized the ulcer healed rapidly.²⁰

In a second type of experiment, the feeding of large quantities of acid after a gastro-enterostomy had been performed²⁰ led to no pathologic lesion. Apparently the alkali of the intestine could neutralize the excess. But if an entero-enterostomy was added to the foregoing procedure then a gastrojejunal ulcer often resulted. It is probable that the anastomosis between the loops of the jejunum deflected the alkali from the gastro-enterostomy stoma.

17. Robertson, H. E., and Hargis, E. H.: Duodenal Ulcer: An Anatomical Study, *M. Clin. N. Amer.* 8:1065 (Jan.) 1925.

18. Bickel, A.: Beobachtungen an Hunden mit extirpierten Duodenum, *Berl. klin. Wchnschr.* 46:1201, 1909. Mann, F. C., and Williamson, C. S.: The Experimental Production of Peptic Ulcer, *Ann. Surg.* 77:409 (April) 1923. Mann, F. C.: Production and Healing of Peptic Ulcer, *Minnesota Med.* 8:615, 1925.

19. Mann (Footnote 18, third reference).

20. Exalto: *Ulcus Jejuni nach Gastroenterostomie*, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* 23:13, 1911.

The feeding of acid was also studied in a different manner. After the production of an experimental ulcer by a vast variety of means it has been found that spontaneous healing rapidly follows. After producing such a lesion in monkeys, Bolton²¹ added hydrochloric acid to their food. As a result healing was delayed to two or three times the normal period. If in addition the pylorus was partially obstructed the delay was still more marked. He also found that foods which caused a relatively longer presence of hydrochloric acid in the stomach caused a proportional delay in healing. Thus on a milk diet ulcers were found to have healed on the twentieth day, whereas on a meat diet after the same length of time there was still a large epithelial defect. Some other experiments of Bolton should be mentioned. He prepared a toxin from the gastric wall which on intravenous injection was followed by an acute gastric ulcer, but only when acid was present in the stomach. If all the acid was neutralized by the oral administration of alkali, then no ulcer followed.

It may perhaps be asked why pepsin rather than hydrochloric acid has not been held accountable. But pepsin, of course, even if its proteolytic action is an important factor, can only act in the presence of acid, and therefore the acid remains a *sine qua non*.

As matters stand now, I believe it fair to say that clinical and pathologic observations of gastric and duodenal ulcers in man justify the working hypothesis that acid is a necessary element in their production, and that the experiments in animals lend support to that view.

ACID CONDITIONS IN GASTRIC AND DUODENAL ULCERS

Acidity Accompanying Gastric Ulcer.—Test meals, both Ewald and Rehfuß, show that in gastric ulcer there is usually a normal acidity. Some cases have a diminished acidity and some an anacidity. In Bell's²² series of observations the percentages happen to be 72 per cent normal, 11 per cent hypo-acidity and 14 per cent anacidity. The patients with the normal percentage do not interest us at present. In them the mechanism for the neutralization of acid proceeds without hindrance. But several questions may be asked concerning those with a diminished or absent finding of acid. In the first place, is this not contrary to our postulate that hydrochloric acid is a contributing cause for the ulcer? We have just seen that an anacidity in the test meal does not necessarily mean that hydrochloric acid is not being secreted. An examination of the chlorides will often show that the anacidity is due to neutralization. I do not know if anyone has investigated the cases

21. Bolton, C.: *Ulcer of the Stomach*, London, 1913.

22. Bell, J. R.: *Gastric Ulcer and Achlorhydria*, *Arch. Int. Med.* 32:663 (Nov.) 1923.

of anacid gastric ulcer from this standpoint, but Apperly²³ studied some cases of anacidity following gastro-enterostomy and found that in these it was due to neutralization. I have little doubt that the same holds true in the cases of gastric ulcer.²⁴ Presumably at the time of the formation of the ulcer free acid is present. It has been shown that many gastric ulcers produce or are accompanied by a diminution in tone of the antrum and a weakened gastric peristalsis. In fact there may be such marked atony occasionally that barium residues persist after forty-eight or seventy-two hours.²⁵ This hypotonia and weakening of peristalsis has been experimentally produced by lesions of the lesser curvature.²⁶ These conditions of diminished pressure on the gastric side distinctly favor intestinal regurgitation, and are sufficient to account for an apparent hypo-acidity, or anacidity. The view of Hurst⁴ that the gastritis that accompanies the ulcer is responsible for a diminished secretion of hydrochloric acid may also be mentioned. We may say then that no one has yet shown that an ulcer may arise in an anacid medium, that all the evidence points to the contrary. When anacidity is present in the test meal, it is probably due to neutralization of secreted acid.

Acidity Accompanying Duodenal Ulcer.—In cases of duodenal ulcer anacidity is exceedingly rare. Hurst⁴ has never observed a case. Nor have I been able to find one in our records. Normal acidity is found in a percentage somewhere around 65, and a hyperacidity in about 35. Of course the actual figures are not so important as a search for the principles involved. We may say again that in the normal cases there is no disturbance in the mechanism for the regulation of the acidity, or at any rate it is insufficient to prevent the acidity from attaining its usual level. The hyperacidity in some of the cases is readily explained. There may be, first, increased pressure on the gastric side tending to hinder regurgitation. Thus a characteristic finding in cases of duodenal ulcer is hypertonicity and hyperstalsis in the stomach. That has previously been mentioned. Second, there may be a lowering of the necessary pressure on the duodenal side. Reference has already been made to this. While there are as yet no experimental observations to substantiate

23. Apperly, F. L.: The Mechanism of Hyperchlorhydria, M. J. Australia 1:33 (Jan. 13) 1923; Achlorhydria: An Investigation into Its Nature with Suggestions for Its Treatment, *ibid.* 2:135 (Aug. 11) 1923; Gastro-enterostomy: Observations on Its Mechanism and on the Production of Pain in Duodenal Ulcer, *ibid.* 1:256 (March 15) 1924.

24. Experiments to test this point are now in progress.

25. Schlesinger, E.: Chronische Gastroparese als Ursache schwerster motorischer Insuffizienz bei freiem Pylorus, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* 32:30, 1920.

26. Klein, E.: Gastric Motility: II, The Conduction of the Gastric Peristaltic Wave, *Arch. Surg.* 12:583 (Feb.) 1926.

this conclusion, it does not seem to me unreasonable to believe that when a severe lesion like an ulcer is present in the duodenum, it will hinder the normal mechanism of regurgitation, whether that mechanism be a general increase of tone, or a retrograde peristaltic wave. Third, a heightened degree of pyloric tone (or pylorospasm) aids both the foregoing factors. Of course it is not necessary that all three of these conditions be present in order to produce a hyperacidity. Also they may vary in degree in different persons and from time to time in the same person.

Acidity Accompanying Pyloric Ulcer.—Ulcers at or near the pylorus are often classified as a third group. They are frequently associated with a hyperchlorhydria, especially when a marked organic obstruction exists. From what has been said above, the reason for the increase of acidity in these cases is obvious and needs no detailed explanation.

PROBLEM OF HEALING

The reparative powers of the organism cannot heal all peptic ulcers. Our views as to whether chronic peptic ulcers may be cured without operation may be quite divergent. On two points, however, I believe all will agree. In the postmortem room healed ulcers are occasionally found in which the scar tissue involves the submucosa and muscularis as has been noted by Stewart²⁷ and Hart,²⁸ among others. Evidently this is a healed chronic ulcer. To call it something else is merely rationalizing. This implies that the defensive powers of the organism may, under certain conditions, effect a cure entirely unaided. On the other hand, even the most enthusiastic proponent of medical cures must confess that he cannot cure all ulcers. In these cases the powers of the organism aided by all the skill of the physician are not sufficient to heal the ulcer. That is the significance of the third postulate. But one thing that is often overlooked is that the operative procedure which is most commonly used, namely gastro-enterostomy, depends on the organism itself for the actual cure of the ulcer, and so acts in principle just as the medical treatment does. From the surgical point of view we may term as indirect all those methods, whether they be medical or surgical, which do not deal with the ulcer directly, and which aim so to alter conditions that the natural powers of cure will come into the ascendancy.

I do not propose at present to consider the exciting cause of the ulcer. To do so would in the present state of our knowledge mean the enumeration of many theories. For purposes of discussion let us call this exciting cause *x*. In view of what has gone before we may

27. Stewart, M. J.: The Healing of Gastric Ulcer, Brit. M. J. 2:1164 (Dec. 16) 1922; The Pathology of Gastric Ulcer, *ibid.* 2:955 (Nov. 24); 1021 (Dec. 1) 1923.

28. Hart, C.: Ehreungen und Betrachtungen über das Geschwür des Zwölffingerdarmes, Mitt. a. d. Grenzgeb. d. Med. u. Chir. 31:291, 1919.

now say that peptic ulcer arises in a predisposed person when acid is present in the stomach and when the exciting cause, which we have called x , occasions it. No doubt, some would prefer to replace the acid factor by the broader term "local predisposing causes," so that it could include traumatic and other agents and the short straight vessels on the lesser curvature. I have no objections, provided we remember always that the acid is an essential element.

Against these factors producing ulcer are arrayed the opposing forces of the organism. It is necessary to divide these into two parts, the defensive powers and the reparative powers. Thus it is not always true that when the exciting cause of a lesion is overcome or ceases to act healing will follow. A common example is one of the roentgen-ray lesions. Here the rays cause the initial trauma, which produces an ulcer, but at the same time they may so change the surrounding cells that healing is permanently inhibited. We must, therefore, in our present state of knowledge concede the possibility that even when all the factors which lead to the formation of an ulcer are removed, in some cases healing may, nevertheless, not take place because of permanent changes in the neighboring cells.

Arranging the foregoing statements symbolically, we have,—ulcer results when:

$$x + \text{hydrochloric acid} + \text{individual predisposition} > \text{defensive powers} + \text{reparative powers}.$$

In what we have termed the indirect method of cure, our efforts must be (1) to strengthen the resisting forces or (2) to weaken or abolish one or more of the "ulcer forces." Little work has been done under the first heading although the attempts to treat ulcer by protein therapy and by vaccines may be classified here. If the ulcer is due to bacteria, attempts to increase the resistance would appear to be a fertile field for study, and perhaps furnish the ultimate method of cure for ulcer.

Most methods of treatment fall into the second group, the attempt to weaken the "ulcer forces." Nearly all the medical procedures attempt to diminish or abolish the second of our three factors, the hydrochloric acid. And in the opinion of a host of surgeons the most common surgical procedure, namely gastro-enterostomy, owes whatever efficiency it has to the same reason. Its ability, however, to produce decided and permanent changes in acidity seems very variable.

We must remember, however, that we are dealing not with two factors, but with at least five, and possibly more; further, that these no doubt vary quantitatively from time to time. What has been termed

the "life cycle" of ulcer,²⁹ the periods of healing and breaking down, is probably due to such variations. We cannot, therefore, expect that the removal of one predisposing factor, such as acid, even though the quantitative relations are changed, will *always* result in a cure. And so we see that the most assiduous trial of the indirect methods may result in failure, and all empirical observations of patients entirely agree with these theoretical considerations.

By the indirect methods, then, we cannot at present hope to cure all our patients. This is true because of the considerations just stated and for a second important reason. From the standpoint of the patient, the healing of the pathologic lesion does not necessarily effect in him a cure. Thus, we may conquer an infection in a tendon sheath, but if the patient is left with a stiff finger we can hardly call our effort a cure. In addition to healing the local lesion, we must leave the patient with a gastro-intestinal tract that will function as nearly perfectly as possible.

For the present the ideal method toward which we must strive must, therefore, be a direct method. It should aim to get rid of the ulcer in 100 per cent of the cases. If the ulcer is removed that at once solves the problem of healing. It does not call on the factors of defense, which according to our postulate cannot heal all ulcers. From the surgical standpoint this means excision. In order to prevent a new ulcer our method must then remove as nearly as possible the three ulcer forces. Unfortunately we have no means of controlling the direct cause, or *x*, nor can we as yet abolish the individual predisposing causes. That leaves us to concentrate on the third factor, namely, acid, and our procedure should aim to eliminate it.

Finally, after removing the ulcer and after abolishing hydrochloric acid, we must correct any functional disturbances that have resulted from the ulcer, and leave our patients once more unconscious of the fact that they possess a gastro-intestinal tract. No less than this should be our ideal. To condemn them to a life of inhibitions can never be synonymous with a cure. That is but a confession of our weakness, necessary perhaps in various stages of progress. But it can never be the goal. We should examine all our surgical procedures from the foregoing points of view.

SUMMARY

1. There is an individual predisposition to ulcer. Evidence in favor of such a view is advanced mainly from studies of the autonomic nervous system.

2. Hydrochloric acid is a necessary factor in the production of a chronic peptic ulcer. It is shown that the hyperchlorhydria and

29. Crohn, B. B.; Weiskopf, S., and Aschner, P. W.: The Life Cycle of Peptic Ulcer, *Arch. Int. Med.* 35:405 (April) 1925.

achlorhydria of the test meal may not be a measure of the hydrochloric acid secreted but rather of a disturbed motility of the stomach and duodenum. Pure gastric juice has a free hydrochloric acid of from 95 to 135, and anacidity may be the result of complete neutralization of all acid secreted.

If we call the direct etiologic factor of the ulcer x , then we may say that an ulcer results when:

$x + \text{hydrochloric acid} + \text{individual predisposition} > \text{defensive powers} + \text{reparative powers}.$

The natural powers may in some cases effect a spontaneous cure, and on the other hand in some cases they never do even if aided by the physician or surgeon.

4. From the surgical point of view all those methods may be termed "indirect" which do not deal with the ulcer directly, but which aim to so alter conditions as to bring the natural forces into the ascendancy and thus effect a cure. At present nearly all the indirect methods whether medical or surgical seek to do this by diminishing the acid factor.

5. Since only a direct method, that is, a method which at once solves the problem of healing by excising the ulcer, can at present approximate an ideal percentage of cures, the ideal method should include such a procedure.

6. The prevention of a recurrence of the ulcer should be attempted by permanently, if possible, altering the values of the foregoing equation, for instance, by the elimination of the hydrochloric acid.

7. At the same time the gastro-intestinal tract must be left in a functionally adequate condition.

A REVIEW OF UROLOGIC SURGERY

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LOS ANGELES

KIDNEY

Surgical Treatment of Nephritis.—According to Kümmell,¹ Harrison in 1896 undertook the first operative attack on nephritis. Israel reported fourteen cases in 1899 in which nephrectomy had been performed for bleeding and renal pain. In 1901, Edebohls advocated the operation of decapsulation of both kidneys as a therapeutic measure in chronic nephritis. Following this work, numerous articles have appeared from time to time reviewing experimental work on animals and clinical results in human beings. Kümmell feels that the clinical results argue in favor of the procedure in spite of the fact that the experimental work is somewhat controversial. The good effect of decapsulation is probably due to the removal of the sympathetic nerve fibers which are severed from the kidney by removal of the capsule. The establishment of collateral circulation and the formation of a new capsule, which takes place rather readily, can only in part account for the favorable results.

Two procedures are most often applied, nephrotomy and decapsulation, while nephrectomy is less frequently performed. Kümmell reviews the clinical results of these operations in the several forms of nephritis. The acute nephritides are first considered. The nephritis of scarlet fever presents a type of renal swelling comparable to glaucoma in the eye. A case is cited in which unilateral decapsulation in an anuric patient led to diuresis and ultimate cure. Nephritis following poisoning, such as occurs after taking mercury, has been relieved in four of twenty-five reported cases in which decapsulation was carried out. Edebohls first employed decapsulation in the nephritis associated with

1. Kümmell, Hermann: Die chirurgische Behandlung der Nephritis, Ztschr. f. urol. Chir. 17:26-52, 1925.

eclampsia, and good results following the operation under such conditions are numerous. Acute infectious nephritis in which the kidney is riddled with multiple small abscesses (which Kümmell speaks of as "nephritis apostematosa") presents a problem. Kümmell feels that in such cases decapsulation or nephrotomy should be performed when the diagnosis is definitely established. The procedure of choice depends on the condition of the kidney and will have to be determined at the time of operation. Of thirteen cases handled by the conservative method of decapsulation, cure was effected in twelve. Trench nephritis in its more severe aspects, especially when hemorrhage, oliguria and uremia are impending, may frequently be brought to a favorable turn by decapsulation, and Kümmell feels that war surgeons were too slow in adopting the method. In considering the chronic cases great stress is placed on the favorable results in so-called nephritis dolorosa, or nephralgia. This group of cases is not scientifically defined, the chief symptom being pain in the renal or ureteral region with few or no clinical pathologic observations. Usually the disease is unilateral. There may or may not be slight diminution of function in the affected kidney, but on the whole the diagnosis rests mostly on the absence of demonstrable pain-producing renal disease. Kümmell recommends decapsulation in such cases and cites numerous instances in which it has afforded relief. The hemorrhagic nephritides constitute another group of cases in which surgical intervention may be undertaken. Particular attention is paid by Kümmell to the cases of essential hematuria. He reviews the present day ideas on the subject and reports his operative experience. Of forty-two cases in which operation was performed, nine were associated with nephritis dolorosa. Nephrotomy was performed in fifteen, nephrectomy in three, and decapsulation in twenty-four, in four of which the operation was bilateral. Of the twenty-four patients, fifteen were discharged as almost cured, eight as improved, and one died fourteen days after operation from pneumonia. Thirteen of the twenty-four cases were traced. In only two of these was there further bleeding.

The cases of chronic interstitial nephritis form a more debatable group for surgical intervention. However, the work of Edebohls, Quiteras, Oliver and Volhard is cited as being evidence of the value of the operation of decapsulation. Rovsing's² report of operation in 157 cases, of which seventy-seven were his own, is encouraging. Thus, fifty-three of sixty-two patients with interstitial nephritis were cured, eighty were improved and one died. Of fifty-six patients with granular nephritis twenty-four were cured, twenty-one were improved, two

2. Rovsing, T.: *Chirurgische Behandlung der Nephritiden*, Ztschr. f. urol. Chir. 15:210-211, 1924.

manifested no change and nine died. Eight of twenty-four patients with nephrosis were cured, nine were improved, four showed no change and three died. Of nine patients with glomerulonephritis, four were cured, four were improved and one showed no change. Six patients with orthostatic albuminuria were cured. The follow-up records of eighty-eight of Rovsing's cases showed complete cure in forty-three after from five to twenty years, improvement in thirty-eight, and no change in seven. In Kümmell's clinic, forty-seven patients with medical nephritis were operated on; unilateral decapsulation was performed in twenty-eight cases, and bilateral decapsulation in five. Ten of these patients died after a short period of improvement, twelve were cured, eight were discharged improved and three were unimproved. Nephrostomy was performed in nine cases with death in two, no relief in two, and cure or improvement in five. Nephrectomy was performed in five cases with cure in three and no relief in two. Thus, of forty-seven patients who underwent operation, eighteen were cured, eleven were improved and five manifested no change; of the thirteen who died, one underwent nephrectomy eight months after operation, during which time he had been able to work. Kümmell concludes that the operative treatment in many forms of nephritis is followed by good results in many cases.

[ED. NOTE.—This article by Kümmell and that by Rovsing, appearing from two different parts of Europe in the same year, suggest the interest that is taken in decapsulation, and should encourage surgeons and internists in this country to attack nephritis by this method more frequently. Probably decapsulation is effective because it in part removes the nerves from the kidney as renal sympathetic neurectomy does. Rovsing reports 157 cases of nephritis in which surgical treatment was instituted over a period of thirteen years. The operative procedure carried out in most of his cases was nephrolysis, that is, shelling the kidney out from its capsule of fat and connective tissue. In cases of severe hemorrhagic nephritis, in which nephrectomy is usually believed to be indicated, nephrolysis might be a better method. This operation is carried out through a lumbar incision; the kidney is stripped from its fatty capsule; the membrana propria is lifted up and incised near the convexity of the kidney and stripped off by means of blunt dissection to the renal hilum. A cigaret drain is left in the wound. Moderate drainage of serum for a few days and healing without complication result as a rule. The end-results show healing and improvement in most cases.]

Anomalies.—Schillings³ reports a case of congenital absence of one kidney. This condition occurs in about one in 2,500 persons. About

3. Schillings: *Anomalies renales*, *Le Scalpel*, 1926, no. 9, pp. 193-196.

300 cases have been reported, most of which were discovered at necropsy. Papin has reported two cases in the living subject, but they were not proved by operation. Schillings has seen a similar anomaly in a woman, aged 33, which was diagnosed clinically and confirmed at operation. The patient had two children; she had never been ill until two years before admission, when she noticed a vague pain in the left lumbar region toward the abdomen and the thigh. Cystoscopic examination revealed the absence of a left ureteral meatus. From a diagnostic standpoint, one should in such cases keep in mind the possibility of congenital or acquired atrophy of the kidney, occlusion of the kidney, a kidney without a ureter or a ureter with an extravesical outlet. Papin says that the cystoscopic examination is extremely important and should be repeated several times. If this procedure does not confirm the absence of one ureteral orifice, a Garceau ureteral catheter is inserted in the normal ureter and the bladder drained with a second catheter left in the bladder to make certain that it does not contain urine. This procedure was followed in Schillings' case. The vesical catheter remained empty, the ureteral one giving 198 cc. of urine in one hour and ten minutes and a 60 per cent return of phenolsulphonphthalein. The diagnosis of absence of one kidney was made, but, as the patient complained of persistent pain in the left lumbar region, the area was explored surgically. No kidney was found, either in its normal situation or in the pelvis. Pain was not relieved and could not be explained.

Boss⁴ reports a case of horseshoe kidney diagnosed preoperatively, and he believes that most cases should be diagnosed thus. Israel and others state that most horseshoe kidneys are diagnosed at operation. In the physical examination, palpation gives the best information. The phenomenon of palpation-albuminuria has only a limited value. While cystoscopy and uretral catheterization in themselves are not especially important, pyelography may yield much information, especially as to the shortening and median position of the ureters. The roentgenogram will, of course, be of more value if the connecting bridge can be demonstrated. Additional information can be obtained from bilateral pyelography, since by such a procedure the V-forming axis of the horseshoe kidney as well as the relative position of pelves to ureters can be determined.

[ED. NOTE.—Diagnosis established prior to operation is a distinct aid to the surgeon. Rovsing observed that if the patient is placed so that the curvature of the lumbar spine is increased, or the back muscles made tense, a characteristic pain may be caused which may be relieved when he lies down. This so-called Rovsing sign has not, however,

4. Boss, William: Zur Diagnose der Hufeisenniere, *Ztschr. f. urol. Chir.* 19:15-27, 1926.

proved to be of much diagnostic value. A fused kidney, unless abnormally enlarged, can seldom be recognized on abdominal palpation. Any tumor involving the median-lying segment of a fused kidney will usually present a mass in the umbilical area. Therefore, if a mass is palpable in the middle of the abdomen, the possibility of fused kidney must be considered. Occasionally, with a low-lying fused kidney, a retroperitoneal mass may be felt through the rectum, with the pulsation of adjacent large blood vessels. Fused kidney was observed in several patients with a urinary sinus in the middle of the abdomen anteriorly; these patients had had so-called abdominal abscesses drained elsewhere. Low or median hydronephrotic sacs, or their postoperative anterior sinuses, should suggest fused kidney. In the presence of lithiasis, the resulting roentgen-ray shadow may be in a position more median than is usual with renal stone. It has been our experience, however, that a stone in the fused renal pelvis often casts a shadow approximately in the normal position. With multiple stones, the shadows may extend across the vertebrae. Shadows cast by calcified paravertebral glands, low or median-lying gallstones, and stones in the upper ureter are most easily confused with those of stones in a fused kidney. If the shadow of a stone lies in an oblique angle and extends toward the median line, it should be regarded as suggestive of fusion. Pyelographic evidence alone may lead to the recognition of fusion. Because of the scarcity of definite clinical data suggestive of fused kidney, its clinical diagnosis is usually made only in the course of routine pyelography. The characteristic finding is the inverted relative arrangement of the calices and the true pelvis. Instead of lateral extension of the calices, there is median or cephalad extension due to torsion of the renal pelvis. Also the ureteropelvic angle, which is usually median to the pelvic outline, is situated laterally. Therefore, when the pyelogram shows evidence of renal torsion, the possibility of fused kidney should always be considered. The identification of shadows and the other conditions usually brought out by the pyelogram also afford diagnostic evidence.]

Haas⁵ says that horseshoe kidney is one of the most common renal anomalies. Urinary obstruction is usual and consequently its sequelae, hydronephrosis, pyonephrosis and stone, are frequently found. Tumors occurring in horseshoe kidney are rare and usually occur in the right half of the renal mass. A patient, aged 45, had three different tumors in a horseshoe kidney. He had pain on the right side, fever and hematuria. At one time the hematuria was marked. Cystoscopic examination revealed a vesical papilloma, which was destroyed by fulguration. Because of a large palpable tumor of the right kidney the patient entered the hospital, where cystoscopy revealed a gaping right ureteral orifice

5. Haas, N. C.: Tumoren in Hufeisennieren, *Ztschr. f. Urol.* 19:81-86, 1925.

spurting blood tinged urine. The urine and the function on the left were normal. At operation a horseshoe kidney was found on the right. It was exposed and found connected to the left by an isthmus. The right half was resected. Pathologic examination showed a large hypernephroma of the upper pole, an adenoma in the lower part, and a papilloma in the pelvis.

[ED. NOTE.—Mixed tumors of the kidney are rare. Graves recently reported several cases, and a number have been reported in foreign periodicals. Tumors occur in horseshoe kidneys relatively more frequently than in normally situated separate kidneys. In view of the rarity of renal fusion, the number of tumors reported occurring in horseshoe kidneys is comparatively large. The usually associated urinary obstruction, pelvic distention and infection favor the formation of inflammatory types of tumor, such as renal papilloma, of which several cases occurring in fused kidney have been reported.]

Hellsten⁶ reports a case of resection of the left hydronephrotic half of a horseshoe kidney. The parenchyma of the isthmus was cut along the groove. Hemorrhage was slight and was stopped by a row of catgut sutures. The top part of the ureter was firmly fixed for a distance of 2 cm. to the pelvic wall. Three years after operation the patient was quite well.

There is a marked tendency for horseshoe kidney to become the seat of morbid changes. Hellsten reviewed 107 cases in which horseshoe kidneys were operated on for various diseases (accompanying table).

Cases in Which Operations Were Performed on Horseshoe Kidney (Hellsten)

| Diseases | Cases | Per Cent |
|---|-------|----------|
| Hydronephrosis | 29 | 27 |
| Pyonephrosis | 13 | 12 |
| Nephrolithiasis | 32 | 30 |
| Nephritis, pyelitis, perinephritis..... | 10 | .. |
| Tuberculosis | 9 | .. |
| Tumor | 8 | .. |
| Renal cysts | 3 | .. |
| Trauma, hemorrhage..... | 3 | .. |

It is found that a substantially higher percentage of these diseases is included among those associated with horseshoe kidneys than among those of the normally formed kidney. This applies especially to hydronephrosis. The operations for hydronephrosis, pyonephrosis and stone in the kidney constitute about 70 per cent of all operations on the horseshoe kidney as against 30 per cent of all operations on the normal

6. Hellsten, O. T.: A Case of Hydronephrosis in a Horseshoe Kidney; Heminephrectomy, *Acta chir. Scandinav.* 59:415-426, 1925-1926.

kidney. It would appear that hydronephrosis, from which pyonephrosis may arise secondarily, and nephrolithiasis are by far the most common diseases connected with horseshoe kidney. In rare cases a horseshoe kidney can be recognized by palpation, and also roentgenologic examination (Voorhoeve). If the roentgenogram shows the kidneys to be low, displaced medially, and with one or both of the longitudinal axes parallel to the vertebral column, or even converging downward, this is indicative of the presence of a horseshoe kidney. Voorhoeve suggests the possibility of getting a roentgenologic shadow of the connecting bridge. In this case the diagnosis of a horseshoe kidney is assured. In pyelography the shadows of the pelvis also show displacement in the same direction, namely, downward and medially. If this is shown on one or both sides, and if there are signs of torsion, the pelvic shadow lying with its convex margin directed laterally and calices medially, the possibility of a horseshoe kidney must be considered.

[ED. NOTE.—Hellsten's data show that hydronephrosis and pyonephrosis frequently occur with horseshoe kidneys. The high insertion of the ureter and the sharp ureteropelvic angle provide inefficient drainage for the renal pelvis; this, together with the unsupported and readily distensible pelvic walls, makes dilatation common. Hydronephrosis and its sequelae, infection and the formation of calculus, are the most common conditions requiring surgical treatment. The distention is often tremendous, and may occur in both kidneys; it is manifested by a tense, fluctuating mass in the abdomen near the median line. The mass is generally freely movable, not tender and moves with respiration. Various surgical procedures have been carried out in endeavors to readjust drainage of the distended kidneys, but in most cases complete removal is indicated. Aspiration of the hydronephrotic mass through the abdominal wall may be followed by persistent drainage or a fatal peritonitis. Abnormally situated horseshoe kidneys sometimes become infected with tuberculosis bacilli. The opposite kidney may also be the seat of disease, either infection or calculus formation. The tuberculous infection may extend to the isthmus, but this does not contraindicate radical treatment, although the operation may be complicated by a long standing fistula.]

Tuberculosis.—Joly⁷ asserts that urologists are unanimous in advising early operation for renal tuberculosis. Rafin compiled statistics of 168 patients who had not been operated on, and whose history was traced either by himself or by the patients' physicians. At the time of the inquiry, ninety-one were dead and seventy-seven were alive. Twenty-nine of the first group died within two years from the onset

7. Joly, J. S.: The Late Results of Renal Tuberculosis, *Brit. J. Tuberc.* 19:188-195 (Oct.) 1925.

of the disease, thirty died in the next three years, twenty-seven died between the sixth and the tenth years and only five lived more than ten years. Eighteen of the second group had had the disease less than two years, nineteen had had it between three and five years, twenty-eight between six and ten years, and twelve more than ten years. Rafin also noted the cause of death in seventy-four cases; in only four it was due to intercurrent disease; in the others it was the direct result of either local or generalized tuberculosis. The disease appeared to be more chronic in the female than in the male. The males who died had the disease on an average of three and three-fourths years, and the females five and three-fourths years. The males who did not die had the disease on an average of four years and four months, and the females five years and five months. The difference may be due to the tendency for the infection to spread to the genital organs in the male. Wildbolz compiled information regarding 316 nonsurgical cases of renal tuberculosis; 218 patients were dead and ninety-eight were alive. Ninety-nine of the patients lived less than two years, eighty-six lived between three and five years, twenty between six and ten years, eight more than ten years; in five cases the duration was not noted. With few exceptions all these patients died from tuberculosis. Sixty-eight of these ninety-eight patients still suffered from severe symptoms of urinary tuberculosis. Clinical cures of nonsurgical renal tuberculosis are exceedingly rare. On the other hand, surgical intervention is often successful.

Falci⁸ studied fifty cases of renal tuberculosis in which treatment was given in Marion's service in the hospital Civile; the patients were less than 18 years of age. He found that the disease was less common in the child than in the adult. The frequency increases directly with the age and reaches its acme between the ages of 13 and 18. The comparative frequency of bilateral cases is higher in children than in adults; in the first years of life it is twice as frequent (28 per cent in children and 14.12 per cent in adults). The infection is bilateral in all cases of children from 1 to 6 years; in 50 per cent from 7 to 13, and 20 per cent from 14 to 18. The disease in children is usually rapidly fatal. The prognosis following operation is also bad; Falci found that 44 per cent of children died after nephrectomy; 16 per cent were worse than before operation; no change was observed in 10 per cent, and cures were obtained in 24 per cent. In adults the period of maximal frequency of renal tuberculosis is between 19 and 30 years. Bilateral infection is much less common in adults than in children; it progresses less rapidly as the reaction of defense is more active. The results from nephrectomy are excellent. Hogge reports 56 per cent absolute cures. Falci con-

8. Falci, Emilio: La tuberculose renale de l'enfant (fréquence, évolution, pronostic) comparée a celle l'adulte, *J. d'urol.* 20:301-317, 1925.

cludes, as does Marion, that infantile renal tuberculosis in children is a grave disease, much more serious than in adults.

Tumors.—Laqueur⁹ describes two cases of pyelitis polyposa and comments on the rarity of polyps in the ureteral and pelvic mucosa as compared with the same condition elsewhere. Lebert, Rayer and Albarran have all reported cases. Seven of ten authors believe the condition to be the result of inflammatory hypertrophy; others believe there are no inflammatory changes. Three cases of pyelitis polyposa of the renal pelvis, two in Federoff's clinic, are reviewed. In each instance the condition was associated with stone, which suggests an inflammatory cause. The differences occur in the structure. In one case (Viannay's), the new growth consisted of young connective tissue without evidence of inflammation. In Federoff's cases, it consisted of granulation tissue which changed to firm fibrous tissue toward the center; it was rich in blood vessels; in Federoff's first case, little cell element was present and in the second there was much.

[ED. NOTE.—This discussion of pyelitis polyposa and polypous fibroid brings up the question of the relationship between low grade chronic inflammatory irritation and excessive regeneration of tissue in response to such irritation. Whether such polypoid overgrowths are to be considered true neoplasms or tumors involves the fundamental problem of the cause of neoplasia in general. The modern trend of opinion among pathologists is to assume that most new growths are stimulated to some extent at least by inflammatory or biochemical irritants acting over a long period of time. If this is true, the conclusion that the type of lesion described here lies at the borderline between inflammatory hypertrophy and true neoplasia is probably correct.]

Maybury and Dyke¹⁰ report two cases illustrating unusual manifestations of the power of the papillomas of the urinary tract to spread by implantation. In the first case, the original papilloma occurred in the renal pelvis, and implantation took place on the walls of the resulting hydronephrotic sac. Removal of the affected kidney together with the tumor was followed by the rapid growth of a malignant tumor in the remaining kidney. The urine contained much pus. In the second case, after removal of a simple vesical papilloma, three "graft-recurrences" occurred in three separate places in the tissues of the abdominal wall, appearing in rapid succession after removal of the first one. It is suggested that all three arose from portions of the original tumor accidentally implanted at the first operation. The primary tumor was

9. Laqueur, B.: Ueber polypöse Fibroide des Nierenbeckens, *Ztschr. f. urol. Chir.* 17:205-212, 1925.

10. Maybury, B. C., and Dyke, S. C.: Some Unusual Manifestations of Spread by Implantation of Papillomata of the Urinary Tract, *Brit. J. Surg.* 13:377-385 (Oct.) 1925.

histologically nonmalignant, but the successive recurrences showed a steady progress toward malignancy. It is suggested that the course of these cases offers an illustration of the inhibitory effect exercised by the presence of a primary tumor in the tissues on the rate of secondary growths, and their degree of malignancy.

Hydronephrosis.—When Rayer first described hydronephrosis it was assumed that the masses were voluminous liquid tumors developing in the renal pelvis. Papin¹¹ designates the condition hydronephrosis if the pelvis dilates to a capacity of from 20 to 30 cc. Such small distentions cause intermittent painful crises and the reflex vomiting so characteristic of large hydronephrotic sacs. The renal area appears normal in roentgenograms, but pyelography provokes the crisis. Careful examination of the pyelogram reveals slight variation from the normal. Papin believes that several sources of error could be avoided in making a diagnosis when there is only slight pelvic distention. By passing the catheter too high one may eliminate the kinks or folds of the upper ureter. Slight hydronephrosis should not be confused with ureteropyelonephritis, with which there is atonic dilatation of the upper ureteral segments; usually pyelonephritis may be recognized by pus cells in the urine. The treatment should be conservative, either nephropexy or enervation of the kidney. Papin considers the latter the most satisfactory operation if the hydronephrosis is slight and painful.

Marion¹² divides his cases of slight, painful hydronephrosis into two types. The first type is caused by an abnormal vessel kinking the ureter. Marion has observed fifteen cases of this type in which section of the abnormal vessel cured the patient completely. There is no obvious cause for the second type. Papin believes that enervation or section of the renal nerves would cure the patients, but Marion does not favor this. He believes that enervation may suppress the pain but will not influence the cause of the disease. In nine cases of this type he obtained cure by liberating the ureter at its superior portion and fixing the kidney as high as possible. Marion thinks that some cases are not due to a narrowing of the ureter, but to a too great fixity to the surrounding cellular tissue and to slight ptosis of the kidney.

Mercier¹³ concludes from his experience of the etiology and treatment of slight hydronephrosis that most cases are produced by pelvic or ureteral membranes and lowering of the kidney a distance of from 1 to 2 cm. for some undetermined cause. The juxtapelvic portion of

11. Papin: Les petites hydronéphroses douloureuses et leur traitement, *Presse méd.* 2:1462, 1925.

12. Marion: Le traitement des petites hydronéphroses douloureuses, *Bruxelles Méd.* 5:1412-1413, 1925.

13. Mercier, O.: A propos de la pathogénie et du traitement des petites hydronéphroses dites sans cause apparente, *J. d'urol.* 20:467-482, 1925.

the ureter being fixed by membranes which are probably congenital in origin, the pelvis becomes either horizontal or oblique, and this tends to create a pelvic fundus. As a consequence of this position, the pelvis must increase the power of its contractions in order to empty normally, which in turn diminishes its contractile power; urine accumulates and hydronephrosis results. The surgical treatment should be conservative. One must abandon pyeloplasty and pyelo-ureteral anastomosis. Renal enervation, which is theoretically an efficacious means of relieving pain, is a delicate operation, at times endangering the renal blood supply, especially when there are pelvic adhesions. The operation is still too recently conceived to determine what its late effects on the kidney and pelvis might be. High nephropexy with liberation of the ureter is, on the contrary, easy and efficacious. It is a logical operation because it reestablishes the normal position of the pelvis toward the ureter. In all Mercier's personal cases the cure was complete and definite.

Gérard¹⁴ reported at the twenty-fifth Congress Francais D'urologie a case of "giant hydronephrosis" of the left kidney, which slowly and progressively developed during successive pregnancies. Ureteral catheterization showed that the right kidney was normal, whereas no liquid could be withdrawn from the left side, although the unusual size of this kidney had been ascertained at the time of the last pregnancy. Two hundred cubic centimeters of sodium bromide solution was injected for pyelography. The patient had a severe reaction, which lasted three days and was accompanied by a marked distention of the hydronephrotic sac. The sac evacuated spontaneously and all symptoms disappeared.

White,¹⁵ in a study of hydronephrosis, found that hydronephrosis with dilatation beginning at the ureteropelvic juncture is the commonest form of the disease. It is both congenital and acquired. Dilatation which advances more rapidly in the calices than in the pelvis is often due to obstruction in the lower urinary tract or to stone in the pelvis. Various abnormalities in the development of the kidney and ureters are reported in connection with hydronephrosis; however, it is not fully understood just how much abnormalities act to favor the development of the condition.

In a large proportion of the cases identified in the fetus and young children, and which are undoubtedly congenital, the dilatation is bilateral and often affects one ureter or both ureters; in some fetuses the lumen is completely obliterated. Usually the first manifestations are in adult life, between the ages of 20 and 30. In many such cases, the kidney is in an

14. Gérard, Maurice: *Hydronéphrose géante; incidents consécutifs à une pyelographie*, Presse méd. 2:1463, 1925.

15. White, H. P. W.: *The Pathology of Hydronephrosis*, Brit. J. Surg. 13: 247-279 (Oct.) 1925.

extremely early stage of dilatation. It is therefore assumed that such cases represent the acquired form of the disease. The earliest cases show narrowing of the ureter from chronic inflammation, which appears to be the cause of the dilatation. In all cases, pyelitis and some chronic interstitial nephritis are associated. Exacerbations of the pyelitis will explain the attacks of pain which come on without apparent cause in most cases. Usually there is evidence of the infection, either on cystoscopy or in the urine, during an attack of pain, when there is often increased frequency of micturition; this evidence may disappear with the attack. Chronic or severe acute inflammatory disease in any part of the body, chronic gastro-intestinal derangement and the pyelitis of pregnancy are common antecedents of hydronephrosis.

The Dietl's crises sometimes observed in cases of movable kidney are no doubt due to renal retention, not from an obstructed outlet of the pelvis but from a congested kidney resulting from pyelitis consequent on chronic intestinal trouble so often present with general visceroptosis, of which the nephroptosis is a part. Many cases in which there is a history of repeated crises fail to show any indication of a dilated pelvis on operation. Tuffier, in describing the results of nephropexy for attacks of pain in forty-five cases, could find no evidence of dilatation in thirty-six. Geraghty and Frontz quote the combined data of seven authorities on 4,576 cases. These show that mobile kidneys occur in 20 per cent of women and in 2 per cent of men. They also refer to Kelly and Burnam, who found the mobile organ on the right side in 177 out of 245 cases, on the left in twenty-five, and on both in forty-three. White points out that if mobile kidney were the cause of hydronephrosis we should find an overwhelming number of cases in women, the right and double hydronephrosis being more common than the left. None of these facts, however, has been substantiated, for the disease is twice as common in women as in men; it occurs with equal frequency in either kidney, and it is rarely bilateral. Moreover, mobile kidney is markedly preponderant in the fourth decade while hydronephrosis is usually preponderant during the third decade.

Polycystic Kidneys.—Davis¹⁶ believes polycystic kidney to be the most important congenital defect occurring in the renal organs. This anomaly, like others of the renal organs, may be associated with other developmental stigmas. It may be present in the fetus, in the new-born child, or even in old age as late as the ninety-eighth year. The liver may also be similarly affected. The subjective symptoms are mainly renal insufficiency, hematuria, pain and infection. A mass in the region of one or both kidneys, if nodular, suggests polycystic kidneys. Increase in

16. Davis, J. E.: Congenital Polycystic Kidneys, *Am. J. Obst. & Gynec.* 9: 758-783 (June) 1925.

blood pressure usually depends on the force necessary to propel blood through the vessels which have constricted lumina due to the enlarging cysts. The specific gravity of the urine is usually low. Other symptoms comparable to interstitial nephritis may also be present.

Nephrolithiasis.—Hofmann¹⁷ reports a case of gigantic renal calculus. The patient, a man aged 29, had had symptoms of renal stone for ten years. At operation the renal pelvis was markedly enlarged and the stone was removed through an incision in the pelvis which extended up into the renal parenchyma. The pelvis was drained. The stone was 10 by 18 cm., porous in structure and composed of pure ammonium magnesium phosphate.

Reflex Anuria.—Nicolich¹⁸ reported a case of anuria following the removal of a right pyonephrotic kidney. The left kidney was found to be normal before operation. Catheterization yielded a small quantity of purulent urine. The patient's condition becoming rapidly worse, it was decided to operate, and the remaining kidney was decapsulated. The kidney was slightly enlarged and pale. A microscopic examination of a removed section did not reveal pathologic alterations. In the first twenty-four hours only 180 cc. of urine was passed, the second day, 1,000 cc. and the third day 2,000 cc. Recovery was progressive.

Nicolich concluded that the anuria was purely reflex, on account of the success of decapsulation, the histologic integrity of the left kidney, the normal urine passed after operation, and the excellent general health of the patient. Reviewing the urologist's and physiologist's opinions on the subject, he says that the origin of the reflex is to be found in the excitation of one kidney (renorenal reflex), of a ureter (ureterorenal), or of the bladder or urethra. The paths followed by the reflex are not known. Newrit thinks that it follows the splanchnic nerves, and reaches the medulla by the tenth, eleventh and twelfth thoracic nerves. Zoja thinks that its center is in the medulla between the seventh and eighth thoracic nerves.

[ED. NOTE.—Renorenal reflex has been widely discussed by continental surgeons. Most urologists in this country doubt the existence of such a condition. Usually the cases in which suppression is attributed to a reflex condition can be accounted for by a temporary lesion in the remaining kidney. After the removal of a tuberculous kidney, anuria for several days is not infrequent, and is usually due to a toxic nephritis. In one case in which death occurred following nephrectomy for tuberculosis, necropsy revealed an acute toxic condition without evidence of

17. Hofmann, Willy: Ueber einen Fall von ungewöhnlich grossem Nierenstein, Ztschr. f. Urol. 19:881-884, 1925.

18. Nicolich, G.: Anurie réflexe après néphrectomie pour pyonéphrose. Décapsulation de l'autre rein. Guérison. J. d'urolog. 20:41-46 (July) 1925.

tuberculous infection in the remaining kidney. Not infrequently cases of anuria following nephrectomy are due to a mechanical or obstructive condition in the remaining kidney, which becomes effective on account of the increased activity of the organ. Morris reviewed a group of forty-eight cases of anuria in which no operation was performed, and a group of forty-nine cases in which operation was performed; ten (20.8 per cent) of the forty-eight patients recovered, and twenty-five (51 per cent) of the forty-nine recovered. The return of function in some of these cases after drainage of the renal pelvis is remarkable. In one case at the Mayo Clinic only 25 cc. of urine was passed over a period of fourteen days. After drainage of the pelvis 540 cc. was excreted the first seven hours, and 3,300 cc. the next twenty-four hours.]

Perinephritic Abscess.—Cirillo¹⁹ studied bacteria from pus in five cases of perinephritic abscesses. In some cases the abscesses caused the usual symptoms, increased temperature, pain and swelling; in others there was an acute abdominal syndrome suggesting intestinal perforation. The abdominal symptoms have been well described by Legueu, Papin and others; at times they simulate acute intestinal obstruction or peritonitis. In each of Cirillo's cases, the bacteria were those usually found in the intestine. These, following increased virulence, may sometimes overcome the anatomic resistance of the intestinal coats and reach the perirenal tissue, either by the blood stream or lymphatic ducts. The organism which is best able to adapt its virulence to the new medium spreads rapidly and destroys any other associated organisms. Perinephritis, like appendicitis, may be caused by different bacteria, which are sometimes found in pure cultures; in other cases they are contaminated with other organisms. Usually the infection is multiple. The most important part is played by anaerobic organisms. *Bacillus perfringens* and *Bacillus coprogenes-foetidus* are the most frequent offenders, probably because they are more resistant than the others and adapt themselves quite readily to the conditions of living in the perirenal area.

Hematuria.—Blum²⁰ discussed massive hemorrhage from the kidney without obvious preoperative demonstrable cause. In one case such a hemorrhage was caused by a rare subcapsular myxofibrolipoma; in another the removed kidney showed a thrombosed varix with surrounding hematoma and vascular congestion. In one case of hypernephroma, which had not broken through into the pelvis, there was marked bleeding.

19. Cirillo, Giuseppe: Recherches bactériologiques sur quelques cas de suppuration périrénale, J. d'urolog. 20:462-466, 1925.

20. Blum, Victor: Zur Diagnostik und Therapie renaler Massenblutungen, Ztschr. f. urol. Chir. 17:169-186, 1925.

The pelvis contained a urate stone (the only case of primary stone in the pelvis with typical hypernephroma recorded). Blum considers as possible causes of massive renal hemorrhage: (1) trauma; (2) papilloma and papillary cancer of the pelvis; (3) early tuberculous ulceration involving the papillae (diagnosis difficult); (4) congenital cystic kidney (several cases reported relieved by ignipuncture); (5) hypernephroma (the most common cause), which usually invades the pelvis but may cause hemorrhage from pressure changes in the vessels without invading the pelvis; (6) renal and ureteral stones (rarely causing excessive hemorrhage); (7) nephritis (acute glomerular, scarlatinal, postinfluenzal and arteriosclerotic); (8) floating kidney and hydronephrosis (rare and when present due to sudden extrarenal pressure release with sudden draining of the hydronephrotic or obstructed kidney; this develops pressure changes in the blood vessels, which may cause vascular rupture), and (9) essential hematuria.

Blum analyzes the theories and various explanations of essential hematuria, and attempts to show that they can all be made clearer. Kretschmer's classic review of 129 cases is mentioned as evidence of focal glomerular nephritis being a cause in many instances. The experience of J. Israel; Zinner and Rubritius points to atypical nephritis, Fenwick operated in a case showing angioma of a renal papilla. Hofmann found the cause in a small papilloma a few centimeters from the ureteral orifice. Withney's case was explained by a papillary varix. In short, Blum holds that essential hematuria is not a good diagnostic term, and that the conception of an angioneurotic hemorrhage or unilateral renal hemophilia is not likely to be the correct explanation in the majority of cases.

[ED. NOTE.—Few will disagree with Blum's list of causes of massive renal bleeding. The most important remaining point is to explain the essential hematuria group. It is true that the term "essential hematuria" is used too often to cover cases improperly diagnosed, but, on the other hand, there are many cases in which sufficient abnormality will not be revealed by cystoscopy, operation or necropsy to convince the pathologist that the cause of the bleeding lies therein. The term, nephritis, itself covers many and confusing conditions both from the anatomic and functional standpoints. So far as we know, no anatomic, histologic or functional criteria are as yet in evidence to account for the group of nephritides which is consistently accompanied by unilateral renal bleeding while the kidney remains in other ways functionally and anatomically approximately normal. Therefore, it would seem better to wait for the true significance of essential hematuria on a pathologic basis before insisting, as so many do, that the term be discarded.]

Blanc²¹ reports several cases of pyelonephritis accompanied by hematuria. He has divided them clinically, into four groups: (1) acute pyelonephritis with cystitis and terminal hematuria; (2) acute pyelonephritis with renal hematuria, the hematuria taking place usually at the beginning of the crisis and lasting a short time; (3) acute hematuric pyelonephritis, in which hematuria is the predominant symptom, and (4) chronic hematuric pyelonephritis. Various bacteria may be the cause of this type of pyelonephritis. The infection, often unilateral, does not seem to alter the value of the kidneys, which later recover their anatomic and functional integrity. A differential diagnosis may sometimes be difficult, particularly if tuberculosis is present. It must be understood that this type of hemorrhagic renal disease is entirely different from what has been erroneously called hemorrhagic nephritis; this is never associated with pyuria. The prognosis is usually favorable, but in certain instances the long evolution and the quantity and frequency of hematuria may alter the patient's general condition and sometimes the kidney itself. Blanc states that simple ureteral catheterization is usually sufficient; the mere catheterization for the investigation of function will often stop a hemorrhage which has lasted for three weeks or more.

Pyelonephritis.—Luchs²² offers a rather ingenious explanation of the mode of infection of pyelitis in pregnancy. He cites evidence to show that the bladders of many pregnant women contain bacteria which have gained entrance by ascending through the short urethra. He further recalls that ureteral reflux is found where the integrity of the ureteral orifice has been upset, or where the nervous or muscular mechanism of the ureter has been disturbed. In pregnancy the bladder is displaced by the growing uterus so that often the trigon lies in a position parallel to the symphysis pubis. Owing to the physiologic dextroposition and torsion of the pregnant uterus, the lower ureteral segment in the region of the iliac artery becomes kinked. Luchs believes that this may at times reach an angle of 90 degrees. Since as a rule the uterus rotates to the right, the lesion is usually on the right side. He shows several excellent cysto-ureterograms of the reflux.

Naujoks²³ in a series of eighty-one cases of pyelitis of pregnancy, found that three women aborted from the third to the sixth month of pregnancy. Thirty-four children were born from the seventh to the ninth months, and forty-three children were born at term. Of the thirty-four born prematurely, two died before birth, thirteen shortly

21. Blanc, Henry: De l'hématurie dans les pyélonéphrites, *J. d'urol.* **20**: 1-19 (July); 125-140 (Aug.) 1925.

22. Luchs, L.: Ueber den Infektionsweg der Schwangerschaftspyelitis, *Arch. f. Gynäk.* **127**:149-169, 1926.

23. Naujoks, H.: Die Aussichten für das Kind bei Pyelitis der Mutter, *Zentralbl. f. Gynäk.* **49**:1136-1139, 1925.

after birth, and two in a few weeks; five grew to maturity, two being normally developed, and three underdeveloped. Two of the forty-three full-term infants died before birth and two postpartum.

The action of the toxins and the spread of bacteria, as well as the irregular fever, must be considered as the cause of premature births. Two cases are cited. In one, that of a dead fetus, there were colon bacilli in the heart blood as well as in the placenta. In the second case, there were bacteria in amniotic fluid, placenta, and in the blood of the umbilical cord, but none in the heart blood. Colon bacillus conjunctivitis was also noted in one fetus.

[ED. NOTE.—This is a convincing and concise review, and indicates the malignancy of the pyelonephritis of pregnancy which is usually regarded as a comparatively innocuous infection. About one third of the eighty-one cases resulted in the loss of the child. Pyelonephritis is comparatively common; many cases are mild and do not cause sufficient symptoms to require treatment. The high mortality in this series is in part accounted for by the fact that in the cases reported the infection may have been very severe.]

Typhoid Infection.—Patch²⁴ believes that infection of the kidney by typhoid bacilli is not especially uncommon. Such infection is hematogenous. In many cases in which the bacilli are excreted there is no obvious infection; its occurrence is, therefore, usually favored by some accessory local factor. The disease is usually bilateral, although in both of Patch's cases it was unilateral. It takes the form of cortical and intertubular suppurative processes in the renal parenchyma, with pyelitis. Occasionally ureteritis, cystitis and perinephritic abscess are also present. Miliary abscesses have been common in the acute, fatal cases, and pyonephrosis has occurred in a few. If patients survive the infection for any length of time multilocular pyonephrosis, and occasionally formation of stone, may occur. Multiple ureteral strictures were noted in one case. The infection may occur during the acute stage of the fever, during convalescence, or later. The course may be acute, but if the patient survives the condition may become chronic. Recovery was noted in only five of the cases of pyonephrosis, all unilateral and following operation. The symptoms in no way differ from those of other renal infections, and the diagnosis should offer no difficulties if modern methods of urologic examination are employed. Epidemiologically, patients with acute and chronic typhoid infection of the urinary tract are typhoid carriers and are even more dangerous to the community than patients with typhoid infection of the gallbladder.

24. Patch, F. S.: Typhoid Infections of the Kidney, *J. Urol.* 14:199-221 (Sept.) 1925.

Renal Enervation.—Serés²⁵ advises section of the renal nerves in certain diseases, such as slight hydronephrosis, in painful cases of nephritis and nephritis hematurica. He makes an ample lumbar incision, exposes the kidney and separates it from the renal fat. The renal pedicle is isolated so that its elements are completely visible. The anterior and posterior pedicular nerves are isolated and divided, and a partial decapsulation of the kidney performed. Serés has performed the operation in a number of cases, in the majority of which there was relief from pain. Because of one fatal case he has given up the operation, but he believes that if further studies show which nerves may be sacrificed and which should be preserved, the operation may be used again with great benefit.

[ED. NOTE.—The operation of renal sympathectomy seems to be gaining ground among the European surgeons. Doubtless it has been stimulated by Leriche's work on periarterial sympathectomy. Milliken and Karr in this country have definitely shown that the nerves may be stripped from the renal pedicle with little or no permanent damage to renal function. This is somewhat in conflict with Serés' statement, based on the work of Bellido, that renal denervation, if bilateral, will lead to renal insufficiency and death of the animal. The work of Boeminghaus supports the contention of Milliken and Karr that experimentally bilateral denervation may be done without any permanent damage. The clinical picture of nephritis dolorosa and nephralgia is being more and more talked of in urologic literature. Of the actual motor mechanism of the function of the renal pelvis and ureter, its ability to go into nodal spaces with transient pelvic or ureteral dilations, we know little. We do know that pain in the renal area without demonstrable renal lesions, and pain in the course of the ureter without stone or gross infection, may often be relieved by decapsulation of the kidney or by dilating the ureter with bougies. Hunner would probably feel that most of these cases belong in the ureteral stricture group and treat them by dilatation; Ambard and Papin, Legueu and Flandrin, Rovsing and Kümmell decapsulate the kidney or perform renal sympathectomy, and the results are good. Probably these methods will be adopted more universally in America, and in the next few years we shall have more clinical experience to help us in deciding the value of such procedures.]

Andler²⁶ concludes, from a careful and detailed study of clinical and experimental data, that after destruction of the nerve supply of the renal pelvis and ureter atony and dilatation result with consequent

25. Serés, Manuel: Enervation der Niere, *Ztschr. f. urol. Chir.* **17**:54-56, 1925.

26. Andler, Rudolph: Die Atonie des Harnleiters mit Dilatation und Hydronephrose, ihr klinisches Vorkommen und ihre tierexperimentelle Erzeugung, *Ztschr. f. urol. Chir.* **17**:298-357, 1925.

dynamic interference with the urinary outflow. Denervation of the renal pelvis and the entire ureter by itself does not bring about a disturbance of peristalsis. However, denervation of the renal pedicle causes the appearance of atony and dilatation of the pelvis and ureter. During denervation of the renal pedicle, as a rule there is an increase in the strength and frequency of the contraction of the renal pelvis and of the ureter. After complete denervation there is paralysis of the pelvis and ureter. Peristaltic movements cease entirely.

The dynamic interference with the urinary outflow is most marked in the first few days. If bilateral denervation is carried out at the same time the animal usually dies in uremia. The same result is obtained if one side is denervated and the opposite ureter is ligated. If bilateral denervation is carried out at different times, allowing an interval of a number of days, the animal usually lives. The urinary drainage on the denervated side undergoes improvement after a few days, and this increase continues up until about the fourteenth day. Then the lessened urinary outflow persists below normal. The peristalsis does not completely return to normal, and the propulsive force to the urine is insufficient. As a result hydronephrosis and hydro-ureter result.

The application of paravertebral or splanchnic procaine anesthesia, as carried out by Laiven and Neuwirt, temporarily relaxes the ureter in cases of impacted stone.

Andler warns against the possibility of hydro-ureter and hydronephrosis following the operation of Ambard and Papin, in which denervation of the renal pedicle is applied to human beings. The decapsulation operation of Edebohls is recommended as a better procedure in such cases, as it does not seem to have this inherent danger.

[ED. NOTE.—Stimulated by the work of Ambard and Papin, and Flandrin, much work is being done on the renal and ureteral nerve supply, and the need of better means of treating painful kidneys and ureters that show little or no serious lesions is being recognized. The European writers assert that since the war the condition of nephritis dolorosa (a comprehensive though indefinite term) is on the increase.

The operation of renal periarterial sympathectomy, as brought out by Papin, has been regarded as a hopeful procedure to be used in the more difficult and obscure cases. Andler's work, therefore, comes in good time, and if his conclusions prove to be correct this operation will quickly fall into clinical disrepute. One should certainly perform such an operation with the knowledge that nephrectomy may be done safely later if necessary.]

Experimental Surgery.—Carson²⁷ reports his observations in experimental nephrotomies on dogs. He cites the work of Moore and Corbett,

27. Carson, W. J.: *Experimental Nephrotomies*, Surg. Gynec. Obst. **42**:53-57 (Jan.) 1926.

who found that an operation on the kidney damages the kidney, that the suture which controls hemorrhage does more harm than the incision, that the destruction of the kidney extends far beyond the site of operation, and that the functional activity of the kidney is usually reduced. Magoun, who performed experimental nephrotomy twenty-six times on twenty-three dogs, concluded that in fourteen of his experiments there was a reduction in the function of the kidney, which was proportionate to the amount of renal tissue destroyed. Carson found, in sixteen operations on dogs with both kidneys, that the line of incision up to fifteen days measured from 3 to 5 mm. in width, and from fifteen to 266 days it varied from 1 to 5 mm. in width. In nine nephrotomies on dogs from which one kidney had previously been removed, the bleeding time varied from two to ten minutes. Gross examination of this series of kidneys showed the scar to be from 1 to 2 mm. in width. In no instance was there any complication such as infarct, postoperative uremia, stone formation or fistula. In the twenty-five operations performed with interrupted sutures in the capsule, postoperative hemorrhage occurred once. Carson concludes that nephrotomy in dogs with interrupted Cushing sutures in the capsule is apparently a safe procedure. Cessation of bleeding is brought about by the production of a physiologic clot.

Holloway²⁸ performed a series of experiments on dogs in an attempt to determine the effect of diuretics, injected intravenously, on autogenous and homogenous kidney transplants. Autogenous transplants maintain viability and functional activity indefinitely, and the death of the animal or disturbance of function of the transplant is due to extraneous causes. The functional activity and also the secretion of such transplants are apparently similar if not identical with those of a normal kidney. The effect of diuretics is the same as in a normal kidney.

Homogenous transplants maintain only a transient viability, and their functional activity is usually short-lived. As long as they remain viable, they function in a manner similar to autogenous transplants. They tend to eliminate urine that in most respects is similar to urine secreted by normal kidneys. As a rule, however, the early appearance of albumin, red blood cells and pus denotes marked parenchymatous changes within the kidney. While functioning, the homogenous transplant tends to respond to a diuretic in much the same way as does a normal kidney, except that diuresis is not so marked or so prolonged. Loss of function and lack of response to diuretics are apparently directly in proportion to pathologic changes within the transplanted kidney. When function has ceased, the introduction of a diuretic is without effect.

28. Holloway, J. K.: The Effect of Diuretics on Transplanted Kidneys, *J. Urol.* 15:111-131 (Feb.) 1926.

URINARY INFECTION

Antiseptics.—Leonard and Frobisher²⁹ review the essential requisites of a satisfactory internal urinary antiseptic and state that hexylresorcinol most nearly fulfils these requirements. It soon became apparent that certain factors interfered with its antiseptic action. The first of these to be discovered was the administration of sodium bicarbonate, and the second was the routine practice among urologists of forcing fluids in the treatment of urinary infections.

Experimental data are cited which show that it is the surface tension changes and not the changes in the reaction of the urine which result from the administration of sodium bicarbonate that effect the potency of the drug.

Leonard and Frobisher find that the successful application of hexylresorcinol in the treatment of chronic infections of the urinary tract depends, therefore, on the strict observance of four factors, all of which bear a distinct relationship to the surface tension of the urine. The dosage must be adequate (0.6 Gm. three times daily); with smaller doses there may be insufficient reduction of the surface tension of the urine. The fluid intake must not be increased, for this not only dilutes the active hexylresorcinol in the urine but renders even that dilution less effective than it would be otherwise, by raising the surface tension. Sodium bicarbonate must be avoided, for this raises the surface tension of the urine so markedly as to rob it of its bactericidal properties. The course of treatment should be uninterrupted and sufficiently prolonged. The organisms which are most resistant to surface tension changes in the test tube (*Bacillus coli* group) are most resistant to the action of hexylresorcinol in the urinary tract. Chronic *Bacillus coli* infections ordinarily require from sixty to ninety days of continuous treatment on doses of 0.6 Gm. (four capsules) three times a day. Chronic coccus infections, on the other hand, may clear up completely with startling rapidity (forty-eight hours) and ordinarily require less than three weeks of treatment.

Braasch and Bumpus³⁰ review the results of chemotherapy. They find that of the various mediums employed with intravenous chemotherapy, mercurochrome-220 soluble has probably proved to be the most efficient. It is particularly effective in cases of acute and subacute infections of the urinary tract, and it has also been of great value in occasional cases of acute general sepsis of various types. In chronic

29. Leonard, V., and Frobisher, M.: Clinical Application of Hexylresorcinol in Urology, with Observations on the Significance of Surface Tension in Urinary Antisepsis, *J. Urol.* 15:1-10 (Jan.) 1926.

30. Braasch, W. F., and Bumpus, H. C., Jr.: Clinical Results with Intravenous Chemotherapy in Urinary Infections, *J. Urol.* 15:341-349 (April) 1926.

infections involving the urinary tract and other tissues it is not of great therapeutic value. The greatest objection to its intravenous use is its toxicity. Severe reactions are common, marked by prostration, chills and dysentery. Two of the 196 patients who received intravenous injections of mercurochrome-220 soluble at the Mayo Clinic during the last year died. Necropsy in one case demonstrated that, in the absence of any other cause of death, toxemia was the probable lethal factor. It is evident, therefore, that mercurochrome should be used intravenously only in emergency. Although the element of danger is ever present, nevertheless, in cases of acute sepsis, when other measures have failed, it merits trial. The number of spectacular recoveries reported following its use excludes the possibility of coincidence.

Hexamine was used in seventy-six cases of acute and subacute urinary infection, and was found to be useful in controlling symptoms and fever after manipulation in the urinary tract. Fischer's solution (sodium chloride 1.4 per cent and sodium carbonate 2 per cent) intravenously is indispensable in caring for certain cases of urinary obstruction with high blood urea value.

Helmholz and Field,³¹ after extensive experimental study, found in the dosages used that hexamine is superior to mercurochrome-220 soluble and hexylresorcinol as a urinary antiseptic in cases of infection produced by *Staphylococcus albus* and *Bacillus coli*. *Staphylococcus albus* is much more vulnerable to the action of hexamine than *Bacillus coli*.

BLADDER

Tumors.—Damski³² says that radical extirpation of the bladder with implantation of the ureters into the bowel for cancer of the bladder has adherents and opponents, but the mortality remains colossal. The operation of bilateral nephrostomy or ureterostomy is occasionally employed in cases of extensive inoperable cancer. The object of the operation is to relieve the patient of the pain incident to the passage of urine into the bladder and the contraction of the bladder in voiding. It is also thought to lessen the amount of coincident infection. Six cases are reported in which this operation was performed. Four patients were not relieved, and died soon. One was relieved definitely from tenesmus and pain, in spite of the rapid growth of the cancer with pelvic infiltration. In another case catheterization, after deviation of the urinary

31. Helmholz, H. F., and Field, R. S.: The Therapeutic Value of Mercurochrome, Hexamethylenamine and Hexylresorcinol in Cases of Experimental Urinary Infection in Rabbits, *J. Urol.* **15**:351-362 (April) 1926.

32. Damski, A.: Zur Frage der Harnableitung oberhalb der Blase bei inoperablem Blasencarcinom durch Nephro oder Ureterostomie, *Ztschr. f. urol. Chir.* **15**:50-51, 1924.

stream by the method described, yielded great quantities of putrid purulent material. No diminution in pain or tenesmus ensued. The patient died on the eighth day. Damski agrees with Legueu and Papin that the operation is useless, especially in cases in which there is mucopurulent secretion from a bladder that is filled with necrotic detritus.

[ED. NOTE.—Last resort measures for extensive carcinoma of the bladder are usually fruitless. At best improvement is short and hardly commensurate with the pain and suffering incident to the operation. In spite of the high mortality, transplantaion of the ureters, followed by total extirpation of the bladder, is the only procedure thus far advocated that offers a chance of even temporary relief in this type of case. When operation, or a series of operations, of such magnitude is indicated the malignancy is usually so widespread that hope of cure is abandoned, unless the surgeon is totally inconsiderate of operative mortality. A number of cases of complete resection of the bladder have recently been reported from Russian clinics by Federoff and Bystrow. In a series of 321 cases from the literature, the immediate mortality varied from 50 to 60 per cent. Federoff advocates a two-stage operation and an early radical operation.]

Diverticulum.—Jarosz,³³ after discussing the theories of diverticula of the bladder, says that congenital diverticula are usually single, consist of mucous membrane and muscular layers, and communicate with the bladder through a small opening; the musculature around the opening is occasionally strong enough to act as a sphincter. Acquired diverticula occur in later life, usually because of obstruction to the outflow of urine and an area of yielding of the weaker parts of the musculature of the bladder. Acquired diverticula are usually multiple; they consist of atrophied mucous membrane with a thinned-out or missing musculature and communicate with the bladder through a large opening. In spite of size, they may be symptomless for years, and are found only by accident or intervening urinary infection.

In examining the material in his clinic, Jarosz found only nine cases of diverticula among 181 cases of prostatic hypertrophy, sixty-one of tumor of the bladder, twenty-four of vesical calculi, and thirty of other vesical lesions. He believes that the cystoscope is of untold value in the diagnosis of these diverticula, and favors their treatment by radical resection.

Perivesical Infection.—Malatre³⁴ reports the case of a man, aged 67, who sixteen years before had had several slight attacks of hematuria. Recently the hematuria had recurred. He was markedly constipated and

33. Jarosz, H.: Zur Kenntnis der Harnblasendivertikel, Ztschr. f. Urol. **19**: 722-733, 1925.

34. Malatre, J.: Un cas rare de péricystite suppurée chez un vieilil urinaire, J. d'urol. **20**:320-323, 1925.

had severe pain after urination. Cystoscopic examination revealed that the dome of the bladder was congested, and that there was bullous edema in the base, which was dotted with small nodules. The urine became more purulent after cystoscopic examination. During the course of a second cystoscopic examination there was a sudden small hemorrhage, followed by fetid cloudy liquid from the base of the bladder. A diagnosis of perivesical abscess was made. The urine became more cloudy, but the patient's general condition improved and the pain disappeared. Three weeks later he died from pulmonary complications. At necropsy, besides the lesions of bronchopneumonia and of bilateral nephritis, loops of the small intestine were found to be attached to the bladder. A small mass was found on the upper surface of the bladder; it was about 3 cm. in diameter and was lined by serous membrane and suspended in the abdominal cavity. There was marked infection extending along the ureters, and on the posterosuperior surface of the bladder a cavity was found which contained about 30 cc. of thick, foul smelling pus. This cavity was not lined by mucosa and was situated between the dome of the bladder and the detached peritoneum. It communicated with the cavity of the bladder by an irregular fistula, which opened into the dome. A small concretion was embedded in the peritoneal coat; this had probably been formed in a small cellule or pouch outside the bladder. It became infected and pushed the peritoneum upward and away from the bladder.

Calculi.—Stirling³⁵ asserts that dumb-bell stone of the bladder and diverticulum is rare. He reports a case in which stone had been removed from the bladder in 1918. In 1925 a stone of the dumb-bell type was found, the larger portion being in the diverticulum.

[ED. NOTE.—Urinary obstruction and the sacculation of infected urine are conducive to the formation of calculi. Dumb-bell and hour-glass stones are occasionally seen; generally the larger portion of the stone is in the diverticulum. Diverticulum and stones in the bladder are often associated. Crenshaw and Crompton reported twenty-eight cases in which the two conditions were present. In thirteen cases the stone was in the bladder alone, in nine in the bladder and diverticulum, and in six in the diverticulum alone.]

PROSTATE

Hypertrophy.—Hunt³⁶ classifies the causes of death following prostatectomy in three groups: (1) preexisting and coexisting organic diseases; (2) surgical accidents, and (3) postoperative complications.

35. Stirling, W. C.: Recurrent Dumb-Bell Stone in Vesical Bladder and Diverticulum, *J. A. M. A.* 86:478-479 (Feb. 13) 1926.

36. Hunt, V. C.: Treatment of the Surgical Patient Handicapped by Urinary Obstruction, *Surg. Gynec. Obst.* 42:187-190 (Feb.) 1926.

Many causes of death are preventable. Prostatectomy is never an emergency procedure. In most instances urethral catheter drainage is successful and allows sufficient time to ascertain the physical status of the patient and then to determine the time of removal of the obstruction. The prostate should be removed only after the patient has recovered from the effects of obstruction. Coexisting renal insufficiency and cardiovascular disease are responsible for the majority of deaths following prostatectomy. Urinary retention with resultant renal insufficiency and subsequent uremia directly affect renal function and enhance coexisting cardiovascular and pulmonary diseases. This makes drainage of the bladder the most important treatment preliminary to prostatectomy. Preliminary treatment should be continued until the reaction to renal functional tests approximates normal. Hunt states that in most instances permanent drainage may be obtained through urethral catheterization. This limits the surgical procedure to one operation, which permits exposure, visualization and accurate hemostasis. In 1,783 prostatectomies performed at the Mayo Clinic, preliminary cystostomy was necessary in 437 (24.6 per cent). The mortality rate following prostatectomy at the Mayo Clinic for the twelve year period was 5.5 per cent; the mortality rate for the two-stage operation was 7.5 per cent, as compared with 4.8 per cent for the one-stage operation. The mortality rate following the one-stage operation was lower than that following the two-stage operation, by virtue of the better general condition of the patients selected for this method. The mortality rate following the two-stage operation would have been lower than it was had the two-stage method been employed as a routine in all cases. There were 113 deaths following operation in this series of cases, ninety-nine of which occurred within thirty days after operation. Thirty-three deaths followed two-stage operations; these patients were the poorer surgical risks. Twenty-two patients were prepared by permanent or intermittent urethral catheter drainage; forty-four had no preparation. In 50 per cent of the deaths in which necropsy was obtained death was found to be due to preexisting and coexisting disease; in 4 per cent it was due to surgical accidents, that is, hemorrhage and shock, and in 46 per cent it was due to postoperative complications. In 75 per cent of the deaths occurring when there had been no preliminary treatment, death was due to preexisting and coexisting organic disease. In 437 cases in which preliminary cystostomy had been carried out, the mortality rate was 7.5 per cent for the subsequent prostatectomy. In 666 cases there was no preparation, and the mortality rate was 6.6 per cent. In 680 cases in which urethral catheter drainage had been carried out, the mortality rate was 3.2 per cent. The mortality rate following prostatectomy on the best surgical risks without preparation approaches that of the exceedingly poor risks requiring cystostomy, and is twice that following the preparation of patients by urethral catheter drainage.

Walters³⁷ says that the condition of the patient does not depend so much on elimination from the body by way of the kidney, the intestine and the skin as on what remains in the blood and in the tissues. He reports 204 consecutive operations for prostatectomy, with only three deaths.

Without preliminary preparation, including control of urinary infection, and in the absence of studies of renal function to determine the capacity of the kidneys, the risk of a one-stage operation may be lowered by removal of the prostate through a perineal incision, on account of the dependent drainage and because the perivesical tissues have not been opened to infection. If the prostate is small and prostatitis is marked, the perineal operation may be expected to give good results. Previous operations on the bladder may cause contraction to the extent that the perineal approach to the hypertrophied gland becomes preferable. Postoperative ventral hernia complicating previous operations may favor a perineal operation, which can be performed without fear of opening the peritoneal cavity.

Walters believes that if the patient has been prepared so that prostatectomy can be safely performed it makes little difference, from the standpoint of the mortality rate, whether the gland is removed through a suprapubic or a perineal incision.

Bumpus³⁸ believes that the evidence obtained from cystograms is a reliable indication of the duration of the prostatic obstruction. If the obstruction has lasted for a short time, the deformity of the bladder is slight; if for a moderately long time, the outline is trabeculated and irregular, while if for a longer period, the bladder tends to become cone shaped and irregular in outline and one or more diverticula may be present. The amount of residual urine present indicates the extent of the obstruction. Cystoscopy should be avoided if possible, as the passage of any rigid instrument traumatizes the urethra. Cystoscopy is indicated if the symptoms are out of proportion to the prostatic enlargement. If the prostatic enlargement extends into the bladder rather than into the rectum, the cautery punch operation through the urethra is performed. In cases of impaired renal function with high residual urine the bladder is emptied gradually. Large amounts of fluid are administered by mouth and also by subcutaneous or intravenous injection. Following the administration of fluid, the patient is put daily in a hot pack and a profuse sweat induced. If a urethral catheter is tolerated, the preparation for operation may continue with this form of drainage. If the blood urea

37. Walters, Walzman: *Physiological Principles in the Treatment of Benign Hypertrophy of the Prostate*, Surg. Gynec. Obst. **42**:191-194, 1926.

38. Bumpus, H. C., Jr.: *Preparation of Patients for Prostatectomy*, Surg. Gynec. Obst. **42**:182-186 (Feb.) 1926.

decrease is slow and the patient's general condition is poor, a preliminary cystostomy is performed. With a two-stage operation a blind enucleation is necessary; this is a poor surgical procedure and is inevitably followed by inferior functional results. To undertake cystostomy in the presence of high blood urea is to diminish the possibility of the patient's recovery, since the added load to the reduced renal function imposed by the operation is more than can be withstood.

[ED. NOTE.—Bumpus' data on the value of the one-stage and two-stage prostatectomy are based on an experience with several thousand cases. His statement that the two-stage operation compels a blind procedure reflects the opinion of the Mayo Clinic. In other clinics, the two-stage operation is sometimes performed in such a manner that the second or blind procedure is eliminated, the tissues being well exposed, as in a one-stage operation. This, however, has the disadvantage of spreading the infection, which is always present, and sometimes of tearing the peritoneal fold. One of the most common causes of death in two-stage prostatectomy is peritoneal infection from a tear in the peritoneum. The one-stage visualized operation unquestionably gives a better functional result, but the average operator secures a lower mortality rate by the two-stage procedure.]

Von Illyés³⁹ calls attention to the frequency of recurrence of hypertrophy in nodes of prostatic tissue left at the first operation, and believes it is important to remove the prostate in one piece and to look over the field before finishing the operation, in order that no segments are left.

The familial tendency to prostatic hypertrophy is discussed. In one instance in von Illyés' series, a father and five sons had the disease.

In considering tests of renal function, von Illyés believes that Ambard's coefficient is untrustworthy. He relies more on the blood urea and the rest nitrogen as indexes of renal function. The borderline of operability in cases with renal impairment, when conditions fail to respond to drainage and return approximately to normal, is difficult to delineate. The blood freezing point is of great help, according to von Illyés; when it sinks to from 60 to 67 degrees below zero, the operation cannot safely be undertaken. In each case the general condition of the patient should be the criterion on which the surgeon must base his judgment. The presence of a firm node in the enlarged prostate is an indication for operation, as this may signify cancer or, sometimes, nonmalignant fibro-adenoma.

Thirty-nine deaths in von Illyés' series of 470 cases in which operations were performed are recorded. In the last 330 cases he used

39. Von Illyés, Géza: Ueber einzelne Fragen zur Therapie der Prostatahypertrophie, *Ztschr. f. urol. Chir.* 17:229-242, 1925.

regional anesthesia of the epidural or caudal type. The technic of caudal block with infiltration to the abdominal wall is described. This has greatly reduced the operative mortality.

The suprapubic operation and the placing of a tampon and drainage tube in the prostatic fossa are described. The drain is usually removed on the fifth day. An indwelling catheter, placed at the time of operation, permits drainage and lavage of the bladder. The urethral catheter is removed about the twelfth day. Von Illyés cautions against exposure during operation of the prevesical space and consequent infection. In five cases of diverticulum of the vesicle, the sac was resected at the time of prostatectomy, with suture of the wall of the bladder.

Pericystitis is regarded as a serious complication. Epididymitis tends to appear about the second week, especially if the catheter is left in and there is marked urethritis.

The postoperative incompetency of the internal sphincter and the dilatation of the prostatic fossa, forming a sort of forebladder, are mentioned. Here necrobiotic tissue may become incrustated and cause persistent pyuria and dysuria, which can be relieved only by removal of the calcareous granulation tissue. This can be accomplished by means of the cystoscopic rongeur.

Distended and painful seminal vesicles are indicative of carcinoma in many instances.

Von Illyés favors a one-stage operation.

[ED. NOTE.—Von Illyés' conclusions are in accord with those usually held by modern urologists of experience. There is some dispute as to the type of treatment of the prostatic fossa after prostatectomy, that is, whether it shall be merely sutured, or packed with gauze (around a drain or catheter), or distended with an apparatus such as the hydrostatic bag of the Hagner-Pilcher type, and when and how, and how long, to leave in a urethral catheter. Each of the methods is fraught with many possibilities for good or bad. The one significant feature of the Young perineal operation is the packing of the prostatic fossa from below and exterior to the capsule, as a means of hemostasis. This, it is believed, gives less chance for the development of the hour-glass bladder-prostatic urethra and wide stretching of the prostatic fossa.

As a matter of fact, the control of bleeding from the fossa after operation is not yet a perfected procedure. Each of the methods mentioned is widely used and usually successful. In general, the hydrostatic bag is the most accurate procedure for hemostatic control. The removal of the bag and insertion of the urethral catheter in one procedure simplifies the early postoperative treatment, and is usually the best plan for the surgeon.]

Keyes⁴⁰ reports an operation for the relief of incontinence following perineal prostatectomy. The perineum was opened in the line of the old scar, and the rectum separated from the urethra. There was almost complete destruction of the external urethral sphincter. As there was no other method of bringing pressure on the urethra, Keyes attempted to bring muscular pressure by suturing the two levators with the posterior part of the bulbocavernosus. The three muscles were brought together with chromic catgut by three interrupted sutures. They made a muscular bed, the bulbocavernosus holding the two levators snugly forward under the membranous urethra, on which the natural tension of the levators gave an upward tug. Keyes' theory was that the difference between complete incontinence and complete dryness is not the difference between a widely open faucet and a tightly closed faucet, but rather the difference between a faucet that drips very slightly and a tightly closed faucet. Consequently one may expect, occasionally at least, to close such a dripping urethra by relatively slight or indirect muscular pressure. Seven months after operation the patient had recovered completely from the incontinence; he did not arise at night; there had been no leaking in several months.

Malignancy.—Bumpus⁴¹ reports five cases of sarcoma of the prostate. The type of sarcoma and the age of the patient largely determine the physical characteristics of the tumor. Thus, a lymphosarcoma, composed almost entirely of a single type of rapidly growing cell and having little or no connective tissue stroma, will usually be felt as a soft boggy tumor of considerable size, often confused with prostatic abscess. A rapidly growing lymphosarcoma was seen in a young adult. The same type of tumor in another case, that of a patient aged 64, gave an entirely different physical appearance, being described as of uniform enlargement, hard, tense and adherent. The presence of lymphosarcoma was not suspected until discovered microscopically. These two cases of lymphosarcoma illustrate the influence of age on the appearance of the tumor: the younger the patient the more rapid the growth of the tumor, and hence the less dense its consistency. In youth, and in middle and old age, therefore, the same type of tumor may present entirely different physical aspects. In a third case, that of a patient aged 69, the tumor had been regarded for three years as carcinoma of the prostate and was so treated because of its hard nodular feel. Yet, when just prior to death an operation for the relief of obstruction became necessary, examination of the removed tissue showed that the tumor was a

40. Keyes, E. L.: An Operation for Incontinence of Urine Following Perineal Prostatectomy, *Surg. Gynec. Obst.* 42:423 (March) 1926.

41. Bumpus, H. C., Jr.: Radium and Roentgen Ray in the Treatment of Sarcoma of the Prostate, *J. Urol.* 14:519-533 (Nov.) 1925.

fibrosarcoma. A tumor composed so largely of fibrous tissue in a patient nearly 70 was naturally firm, resistant and hard and, without microscopic examination, impossible to distinguish from carcinoma. At the other extreme is a case of myxosarcoma, in a child of 3, which is the large, soft tumor usually associated with sarcoma. Intermediate in physical characteristics is a case of myosarcoma occurring in the sixth decade. As one would expect, the tumor was firm and elastic, but had neither the doughiness of the myxosarcoma nor the firm resistance of the fibrosarcoma. Before the introduction of radium the fatal course of the disease was rapid, and patients did not recover following surgical intervention. According to Bettoni, in twenty recorded surgical cases only two patients lived longer than two months. With radium treatments the results have improved. Young⁴² reports two clinical cases so treated. One of these patients had lived four years, the other nine months. In both the huge mass, diagnosed as sarcoma, and which nearly obstructed the rectum at the initial examination, had entirely disappeared.

Gayet and Peycelon⁴³ conclude from a long and careful study of the treatment of cancer of the prostate that radium therapy has not given the results which were expected at the beginning of its use. The cause remains chiefly in the late diagnosis, the deep location of the lymphatics invaded by the neoplasm, and the difficulty of its application. The surgeon's duty should be to make an early diagnosis and to operate early. If the condition is too far advanced radium should be employed in an endeavor to check the lymphatic invasion as far as possible; if the bladder or the pelvis is invaded, radium is contraindicated. The patient may get relief from pain and may get prolongation of life by palliative operations, such as cystostomy. Radium in cases of extensive growths is dangerous and may induce early metastasis, septic absorption or severe pain.

42. Young, H. H.: *Practice of Urology*, Philadelphia, W. B. Saunders Company, 1926.

43. Gayet, G., and Peycelon, R.: *Contribution a l'etude du traitement du cancer de la prostate*, Arch. franco-belges de chir. 28:759-781, 1925.

Correspondence

"FRACTURE OF THE HEAD OF THE FEMUR"

To the Editor.—Christopher's valuable case report of fracture of the head of the femur¹ in the May issue has been read with interest, most especially the careful survey made of the literature. He states that reports of only fourteen previous cases were found, and he adds one, concluding that this is a rare injury. We did not realize that this was the case, as two instances of this injury have come under the observation and care of one of us (C. W. P.). The apparent rarity of the lesion, however, would seem to warrant putting these two cases also on record. The second of these patients was admitted to the orthopedic division of the Henry Ford Hospital a little more than a year ago and was treated by the other author, whose detailed report on this patient appears here.

The first patient was admitted in the service of Dr. Z. B. Adams at the Massachusetts General Hospital, Boston, in 1920, and this case is reported here with his permission. The patient, Mary M., a rather stout woman of about 45, was riding in the back seat of a small automobile when a head-on collision occurred. (It may be interesting to note that her sister, sitting beside her, suffered a fracture of the posterior upper quadrant of the acetabulum, with a dorsal dislocation of the head of the femur without fracture of this bone, and later was operated on by Dr. Adams, with a successful outcome.)

The accident occurred almost 150 miles from Boston. A surgeon at the scene of the accident diagnosed the dislocation, but, an attempt at reduction being unsuccessful, sent the patient to the hospital the next day. Physical examination on her arrival showed the deformity and other usual signs of dislocation, but roentgen-ray examination also showed a fracture; a fragment comprising about one fourth of the head of the femur attached to the ligamentum teres remained in the acetabulum. Under general anesthesia, Dr. Adams reduced the dislocation without difficulty, and the limb was put up in plaster in the abducted position for two months. Roentgen-ray examination then showed that the fragment had fitted into its normal position in the head, and had remained so after the removal of the cast at the end of two months. Subsequent observation by Dr. Adams showed permanent union to have taken place and excellent function regained.

The second patient was treated, as stated, in this clinic. This patient was first seen, Nov. 20, 1924, the day of his accident. He said that while driving a small car he had crossed the middle dividing line of traffic, and had been hit by a car coming from the opposite direction. This caused his car to come to a sudden stop. His knees hit the dashboard and remained at a fixed point, while his body continued forward until arrested by the resistance of his hip joints. When admitted to the clinic, he complained of severe pain in the region of the left hip and that he was unable to bear weight on this leg.

1. Christopher, Frederick: Fractures of the Head of the Femur, Arch. Surg. 12:1049 (May) 1926.

Under ethylene anesthesia, the dislocated hip was reduced, the closed method of Bigelow being used. A Thomas knee splint was applied with traction in a position to hold the leg abducted 45 degrees and flexed 30 degrees at the hip joint. This position was considered the most advantageous to bring the small fragment in apposition with the remaining portion of the head, by putting the inferior part of the capsule on tension. To prevent the formation of



Fig. 2.—Left hip after reduction, showing line of fracture of head of femur and fracture of posterior upper quadrant of the rim of acetabulum.

intracapsular adhesions by the increased relative degree of mobility allowed, a Thomas splint was used at this stage in preference to a plaster spica.

After a period of six weeks, so that he could be treated as an ambulatory patient, a plaster hip spica was applied from the level of the eighth rib on the right side down to the ankle, with the leg abducted 30 degrees and flexed

20 degrees at the hip, and with the knee flexed 10 degrees. In two weeks, the plaster splint was bivalved laterally and removed below the knee. Massage to the muscles of the hip and knee was begun. Later, baking and passive and active manipulations were instituted to the hip and knee.



Fig. 3.—Right hip for comparative study.

After nine weeks the patient was discharged from the hospital, using a Thomas ring caliper with a Bradford abduction bar attached. In two weeks the abduction bar was discontinued, and a month later the brace was discarded. At this time he was able to walk comfortably with the aid of a cane.

At five months from the date of the accident, clinical examination showed that motions in all directions were to the normal range, with the exception

of complete rotation, which was limited 25 per cent. Exercises to increase this range were instituted. Examination at twenty months after the accident showed that the patient had full range of motion in all directions at the left hip. No points of clinical difference could be found on comparative examination with



Fig. 4.—Left hip twenty months after reduction, showing good bony union and position of fracture of head of femur.

the right hip. Functionally, he was able to use the leg to full capacity without any discomfort. Roentgen-ray examination twenty months after the accident showed good bony union between the fragments and the head of the femur (fig. 4).

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PRIMARY MALIGNANT TUMORS OF THE LONG BONES

END-RESULTS IN ONE HUNDRED AND SEVENTY OPERABLE CASES,
INCLUDING A SMALL GROUP OF MALIGNANT CENTRAL
SARCOMA *

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Periosteal sarcoma of the long bones has long been recognized as one of the most malignant of all tumors. The prognosis in this type has been regarded by surgeons as practically hopeless, even early amputation at the proximal articulation rarely saving the life of the patient. With the advent of the roentgen ray—which was soon recognized as the greatest aid to the surgeon in making an early diagnosis—it was hoped that better results would be obtained by reason of earlier amputation. These hopes, however, have not been realized, and in spite of early amputation, practically all the patients have died of metastases within a few months or a year after the operation.

The end-results of operative treatment of sarcoma of the long bones, as reported at a symposium on long bone sarcoma before the Royal College of Surgeons in November, 1912, and a second symposium before the Association of British Surgeons in May, 1923, showed practically no improvement over the gloomy statistics of Butlin, published a generation ago. A few surgeons, notably Bloodgood,¹ following the lead of Paget and Nélaton, believe that giant cell sarcoma is practically a benign lesion and that these cases should be treated by conservative methods; i. e., preferably curettage, followed by the application of phenol (carbolic acid) and zinc chloride, occasionally by resection and only rarely by amputation. On the other hand, Bloodgood² believes that periosteal

[Ed. Note:—This article, because of its great length, has been divided into two parts; the second part, containing the case reports and illustrations, will appear in the January issue.]

* Read in part before the annual meeting of the Association of British Surgeons, London, May, 1923, and before the American Surgical Association, Washington, D. C., May 5, 1925.

* This series of 170 cases includes periosteal sarcoma, subperiosteal sarcoma, the type of tumor characterized by most pathologists as round cell sarcoma and by Ewing as endothelioma, and a small group of malignant central tumors.

1. Bloodgood, J. C.: *Ann. Surg.* 69:345 (April) 1919.

2. Bloodgood, J. C.: *Am. J. Surg.* 37:105 (May) 1923.

sarcoma is so malignant that amputation rarely saves the life of the patient (probably only 2 per cent of the patients recover) and therefore he seldom, if ever, advises amputation in this type of tumor. Until comparatively recent years, however, surgeons in general have continued to amputate the limb for practically all types of sarcoma of the long bones. With the advent of radium, in sufficient quantities, and further, with the introduction of the high voltage roentgen-ray machine, it was hoped that we should see better results, especially in the osteogenic type of sarcoma of the long bones.

At the Memorial Hospital during the last ten years we have been fortunate enough to have at our disposal an ample supply of radium, and we have made a careful attempt to ascertain the value of this agent in the treatment of long bone sarcoma of all types. During this period, we have been treating different groups of cases by different methods and combinations of methods, i. e., radium alone, roentgen rays alone, toxins alone, toxins and radium, amputation alone, and amputation followed by toxins. (The majority of patients treated during this period have been treated by radium or roentgen rays.) It is the end-results obtained in this series of cases that we desire to report.

At present the surgeons are divided into two fairly definite groups as regards the treatment of sarcoma of the long bones: one group amputates in every case as soon as the diagnosis has been made, regardless of the type of tumor (central or periosteal) or the morphology (giant cell or osteogenic), and the other, never amputating, believes this to be an inefficient and unwise procedure in periosteal sarcoma, as in any event the patient dies; they also believe that central tumors are better treated by conservative methods. If we were suffering from sarcoma of a long bone, we should much prefer to fall into the hands of a surgeon belonging to the first group whose members always amputate rather than of one belonging to the second, whose members never amputate. With the advent of radium and the high voltage roentgen-ray machine, the ranks of the second group are rapidly increasing in number, and fewer and fewer cases of periosteal sarcoma are being subjected to amputation for the reason that strong hopes are entertained that radium or roentgen rays will cure or retard the progress of the disease for a considerable period of time. Whether these hopes are justified, it is, perhaps, too early to say positively, but our results may help to answer the question.

Then there is a third group of surgeons, few in number at present but slowly increasing, who believe that the problems involved in the treatment of sarcoma of the long bones differ so widely that no one hard-and-fast rule that will cover every case can be laid down. This group believes it is wise to make a careful study of each individual case especially as regards diagnosis and to be guided in the selection of treatment to be employed by the results obtained in similar cases.

So far there has been no large series of patients (except those treated by amputation) treated by different methods and traced for a sufficient period of time to permit conclusions of material value to the surgeon. It was in the hope of supplying, in a measure, the necessary data that the present article was written. We believe that a large proportion of patients are now being treated primarily by radium or roentgen rays, and yet the surgeon who advises the treatment probably has no definite idea of the prognosis such treatment offers. He has a fairly firm conviction that amputation offers little or no hope of a cure, and hence he is willing to try any other method that may retard the progress of the disease and possibly save some lives. His decision is based on hopes rather than on facts or any definite knowledge of the end-results of roentgen-ray or radium treatment.

During the last ten years, we have observed a large number of cases in which roentgen-ray or radium treatment has been the primary method of choice and the end-results have been carefully followed up. A distinguished pathologist recently told us that if he ever had a sarcoma of the long bones he would have an immediate amputation regardless of the histologic type of the tumor. Shortly after this a distinguished surgeon made the statement that he had performed his last amputation for long bone sarcoma. In the face of such widely divergent opinions, it is all important that the facts bearing on the diagnosis and end-results of different methods of treatment should be most carefully compiled and published in some detail. It is only by a careful study of these facts that it is possible to form any definite or intelligent conclusions as to the best method of dealing with the condition. At the London symposium on long bone sarcoma in 1923 one of the members stated that long bone sarcoma was so rare that some might question the wisdom of devoting so much time to a discussion of the subject; he estimated that there were only 400 cases in England. While it is true that the condition is a rare one, it is none the less true that when it does occur, it usually occurs in the finest and most healthy specimens of young adult life; therefore we feel stimulated to put forth our best efforts to save these young lives. The very fact of the rarity of the condition has rendered advance in its treatment difficult. The average surgeon may see but one case in a year, or less, and the surgeon of large general hospital experience may see no more than two or three during a year; he does not see enough cases or follow the end-results sufficiently long to enable him to decide from his own experience what method offers the best chance of saving the patient.

The opinions of even experienced surgeons as to the best methods of treating long bone sarcoma are at the present time so widely at variance that the whole subject is in a state of confusion; the result is, that in a given case of sarcoma of the long bones the surgeon is utterly unable to decide what form of treatment to advise.

While the Bone Sarcoma Registry, to which Dr. E. A. Codman has devoted much time and energy for several years, will undoubtedly prove of great help in enlarging our knowledge of the diagnosis and pathology of the disease, so far it has been of little aid in deciding on the best methods of treatment; neither does it furnish any accurate idea of the prognosis of the different types of bone sarcoma. It is quite natural and easy to understand that the average surgeon is far more inclined to go to the trouble of compiling the necessary data (clinical history, roentgenograms, microscopic slides) to register a successful case than he would be to register an unsuccessful one. For this reason, the relative proportion of successful cases in such a collection as the Bone Sarcoma Registry will be greater than the normal rate, as found in a series of consecutive, unselected cases observed at a single clinic or by a single surgeon. This is well shown in the group of giant cell sarcoma. Bloodgood,³ in his latest article on giant cell tumor, has added 100 cases from the Bone Sarcoma Registry to his own personally observed series of cases and uses this compilation to show that giant cell sarcoma is practically always benign. While his statistics may suffice to prove in theory that giant cell sarcoma is quite a benign affair, the memory of the ten patients with tumors pronounced benign giant cell by experienced pathologists⁴ who later died of metastases, and one additional similar case that has likewise proved fatal, has served to convince us that giant cell sarcoma may be a real "specter."

It is interesting to note that the article of McWhorter and MacGuire⁵ containing the end-results of fifty consecutive cases observed at the New York, Presbyterian and Bellevue Hospitals shows almost exactly the same percentage of malignant giant cell tumors as our own series, i. e., one in five.

We cite these cases merely to show that it is impossible to obtain a true idea of the prognosis of bone sarcoma from scattered cases reported in the literature or even from those compiled by bone sarcoma registries. Up to the present time, there has been no large series of cases of bone sarcoma in which treatment with roentgen rays or radium has been systematically carried out in a sufficient number of cases or for a sufficient length of time to permit any conclusions as to the curative value of these agents in bone sarcoma. The unusually large amount of clinical material at the Memorial Hospital supplemented by that of the Hospital for Ruptured and Crippled for more than thirty years has made it possible to

3. Bloodgood, J. C.: Giant Cell Tumor of Bone and the Specter of the Metastasizing Giant Cell Tumor, *Surg. Gynec. Obst.* 38:784 (June) 1924.

4. Coley, W. B.: Prognosis in Giant Cell Sarcoma of the Long Bones, *Ann. Surg.* 79:321 (March) 1924.

5. McWhorter, J. E., and MacGuire, C. J., Jr.: Sarcoma of Bone, *Arch. Surg.* 9:545 (Nov.) 1924.

cases) ; pain appearing several days or weeks before the tumor is noticed and increasing in severity, often becoming worse at night ; an immovable tumor, apparently connected with the bone or periosteum, of firm but not bony consistency ; skin normal in appearance and not adherent, and slight local heat. In the later stages, the skin becomes thin, and the superficial veins are dilated ; but a diagnosis should be made long before this condition is apparent if the life of the patient is to be saved by any method of treatment.

Pain is the first and most important symptom. It nearly always precedes the appearance of a swelling or tumor by a longer or shorter interval—a few days, a few weeks or, in some rare cases, several months. The pain is dull and persistent, often worse at night, and frequently most severe at a considerable distance below the site of the tumor. Early pain before the development of a tumor or swelling has resulted in most of these cases being regarded as of rheumatic origin, and in their being treated accordingly. Severe, persistent pain in any long bone of a healthy, young adult who is between the ages of 15 and 30, especially when it follows a recent trauma, should immediately arouse a suspicion of sarcoma and entitle the patient to frequent physical examinations supplemented by frequent roentgen-ray examination.

A number of pathologic conditions may simulate sarcoma of the long bones more or less closely.

MYOSITIS OSSIFICANS

This condition causes greater difficulty in diagnosis than perhaps any other lesion of the long bones. Fortunately it is a very rare condition. One of us ^a reported several cases and described the differential diagnosis of this condition and sarcoma, at the same time pointing out the fact that in nearly every case it was possible to make a differential diagnosis by the roentgenogram and the clinical history of the case.

The clinical history in a case of myositis ossificans is fairly characteristic ; swelling usually follows a rather severe injury, such as a football injury. The locality of the swelling is most often the region of the quadriceps muscle of the anterior portion of the thigh. The tumor develops rapidly during the first three or four weeks, after which there is a period of apparent quiescence, when there is little noticeable change. Severe pain, which is often associated with periosteal sarcoma, is seldom present in myositis ossificans. In consistency, the tumor is of a peculiar bony hardness in contradistinction to the firm but more or less resilient "feel" of periosteal sarcoma. In myositis ossificans the roentgenogram shows an intact and sharply defined periosteal line, whereas in periosteal sarcoma, even in the early stages, some break in the line will nearly always be noticed, in the way of indentation, or irregularity, or a slight splitting-up of the periosteum. We have observed only two cases of periosteal sarcoma in which the periosteal line was intact. In one of

6. Coley, W. B. C.: *Myositis Ossificans Traumatica*, Ann. Surg., March, 1913.

these cases, which was in an early stage of the disease, it was possible, from the clinical history and in the absence of trauma, to make a diagnosis of sarcoma rather than of myositis ossificans, and this diagnosis was confirmed by microscopic examination. The second case gave a history of an apparently slowly growing tumor of two years' duration following a severe injury. The tumor was situated in the lower end of the femur rather than in the shaft. While the clinical history and roentgenogram pointed to a sarcoma, strange to say, the microscopic sections showed only a productive osteitis or myositis ossificans; this case later proved to be a sarcoma, which metastasized and finally ended in death.*

The rapidity of the growth in periosteal sarcoma varies greatly. The sclerosing type may go on for two or three years or more before attaining a large size; but such cases are extremely rare. On the other hand, the tumor may grow so rapidly as to reach a large size in the short space of three or four weeks, and may destroy the life of the patient in a few months.

OSTEOMYELITIS

In syphilitic osteomyelitis the shaft of the bone is more frequently involved than the extremities, and the lesion is usually characterized by a definite hyperostosis or thickening of a considerable area of the diaphysis. The new bone formation is much more dense than that found in periosteal sarcoma. A type of sarcoma that is usually found in the shaft of the bone in one that has been designated by Ewing as endothelioma with little or no new bone formation; this can be differentiated from syphilitic osteomyelitis in that in the latter condition the progress of the disease is slower, and the pain so characteristic of sarcoma is usually absent. There are certain cases of acute or subacute osteomyelitis which it is almost impossible to differentiate from sarcoma, even with the aid of roentgen-ray examination, and sometimes with the additional help of exploratory operation and microscopic study. Three cases of this kind have recently come under our observation. In none was the correct diagnosis made even with the aid of a careful clinical history and roentgenograms supplemented by exploratory operation and microscopic examination. In two of these cases, the question arises as to whether the original condition might not have been an osteomyelitis, and the sarcoma an independent and later condition superimposed on the original osteomyelitis. We are inclined to believe that the original condition was an atypical sarcoma at least in one of the cases.

In a young man, a primary tumor was removed from the lower end of the femur and pronounced an osteoma; it recurred shortly afterward and ten years later it took on signs of malignancy. It was then possible

*There is another important differential diagnostic feature which previously we have not seen mentioned. Whereas in periosteal sarcoma the roentgen-ray picture shows that new bone or tumor extends around or nearly around, the long bone; in myositis ossificans it is confined to one portion and rarely extends more than one-half the circumference of the bone.

to make a roentgen-ray and clinical diagnosis of sarcoma. Amputation was performed and microscopic examination showed the tumor to be an osteosarcoma with a large amount of ivory-like new bone. In spite of prophylactic toxin treatment, the patient, after remaining well for three years, died of metastases of the lung. In another case, an adult male sustained a fracture of the central portion of the shaft of the femur at the age of 4 years, and another fracture at the same site seven years later. A more or less chronic osteomyelitis developed and continued for nearly twenty-seven years, when a rapidly growing tumor was noted at the same site; this proved to be a periosteal sarcoma. Amputation was performed at the hip joint, followed by prophylactic toxin treatment. The patient is alive and well nine and one half years later (case 18).

In these two cases, we believe it is fair to assume that the old osteoma furnished a favorable soil for the development of a sarcoma many years later in case 1, and in the other case, that a chronic osteomyelitis developed at the site of an old fracture and proved a favorable site for the sarcoma that developed many years later.

TUBERCULOSIS

Tuberculosis of the bones has often been mistaken for sarcoma, and vice versa; yet a careful history and thorough physical examination aided by a roentgenogram should enable one to make a differential diagnosis in the great majority of cases. Generally speaking, the two conditions show striking points of difference as well as similarity. They are both apt to occur in young adults; they have a predilection to the extremity of the bone rather than the shaft; there is often a history of local antecedent trauma in both conditions. They differ in the following important points: Sarcoma, as a rule, occurs in young adults who give every evidence of being in the best of health, whereas tuberculosis of the bones is more commonly found in persons whose general condition is below par. An evening rise of temperature is often noted in tuberculosis of the bones; while it may be noted in sarcoma, it is unusual. The duration of the disease is usually longer and its progress slower in tuberculosis than in sarcoma. Pain may be an important symptom in both conditions but it is usually more severe and persistent in sarcoma. The most important point of difference is the location of the disease: sarcoma practically never begins in the epiphysis of the bone, whereas tuberculosis nearly always begins in the epiphysis and involves the joint in the comparatively early stages of the disease. In tuberculosis, the skin is paler than normal whereas in sarcoma, even in the comparatively early stages, the skin is redder than normal, often of a purple hue, due to dilatation of the superficial vessels.

The diagnosis of tuberculosis cannot always be made from the clinical and roentgen-ray evidence as was pointed out by Beye,⁷ who reported two cases diagnosed as osteosarcoma but which at necropsy proved to be tuberculosis. If these patients had recovered, the claim doubtless would have been advanced that two periosteal sarcomas of the long bones had been cured by the agents employed.

TRAUMA AS AN ETIOLOGIC FACTOR IN CASES OF LONG BONE SARCOMA

Those who still refuse to believe that trauma has an important causal influence on the development of a malignant tumor base their opinion on the theory that the tumor was already present at the site of the injury and had escaped the notice of the patient until the time of the injury. This would assume not only an uncommon ignorance and lack of personal observation on the part of the patient, but in many cases a similar ignorance and lack of observation on the part of the physician who had attended the patient at the time of the injury and who had failed to find any swelling or evidence of a tumor at that time. If a swelling develops at the exact site of an injury, within a few days or weeks or months thereafter, and develops the typical clinical characteristics of a sarcoma, the diagnosis being further supported by microscopic examination, and finally causes the death of the patient, it seems illogical and difficult to nullify or minimize the influence of the injury by the assumption that a malignant tumor was already present at the exact site of the injury but without any previous symptoms or physical signs.

In addition, we have a number of cases in which it is not necessary to decide the question on the powers of observation on the part of the patient or on the part of the physician. The roentgenograms taken at the time of the accident furnish conclusive evidence that there was no pathologic lesion of the bone at the time of the accident, and yet a very malignant sarcoma developed within one or two weeks at the exact site of the injury. These cases, especially cases of recent fracture showing a rapidly growing sarcoma appearing from a few weeks to a couple of months after the injury, furnish, in our opinion, absolute proof that the injury was the causative factor. It is not necessary to be able to explain the exact manner in which trauma may cause the development of a malignant tumor in order to admit its causal influence.

We believe, and more strongly with increasing experience, that all types of malignant tumors are of extrinsic origin. It is not improbable that it may some day be proved that what we have hitherto included under the vague term "hereditary influence" may some day be proved a

7. Beye, H. L.: Errors in the X-Ray Diagnosis of Osteogenic Sarcoma, *Ann. Surg.* 80:730 (Nov.) 1924.

micro-organism or virus, as has already been proved in tuberculosis, and that the only thing inherited is tissues less resistant to the virus or infection. Whether we accept the parasitic theory of cancer or still believe in its intrinsic origin, we must admit that trauma plays a direct and important part in the development of cancer and especially of bone sarcoma. The argument advanced by some writers that, if such were true, all cases of trauma or a larger proportion of cases ought to be followed by the appearance of a cancer, is not logical. If fifty people were plunged into an icy pond and only two developed pneumonia, by the same reasoning we might say that, because forty-eight remained well, the shock and exposure were not causative factors in the development of the pneumonia in the two who contracted it. The exposure to cold simply lowered the resistance of the body and prepared a favorable soil for the development of the pneumococcus.

Since this article was written, the more important work of Gye and Barnard of London has been published, and the micro-organism that they have discovered has been widely accepted as the cause of malignant tumors. The earlier and important research work of Glover and Scott of New York, and Nuzum of Chicago, as well as Young of Edinburgh, furnishes strong evidence in support of this view.⁸

Clinical evidence and experimental researches have shown that trauma is an exciting factor in a large proportion of cases of tuberculosis of the bone. Recently Schmidt has shown that nearly 30 per cent of the cases of acute osteomyelitis have a history of antecedent trauma.

The present series of 170 cases shows a history of definite antecedent local injury in eight-seven cases, or slightly over 50 per cent. This is almost identical with the percentage found by Gross in his series of 160 compiled cases of sarcoma of the long bones published in 1879. Our recent report of fifty cases of giant cell sarcoma showed a history of antecedent local trauma in 56 per cent. Kolodny in his recent paper on bone sarcoma found a history of antecedent local trauma in 70 per cent of patients over 10 years of age.

The interval elapsing between the injury and the development of the tumor is important. In the present series it is shown to be as follows: few days, six cases; one week, five cases; from two to three weeks, twenty-four; from three to four weeks, six; six weeks, one; two months, nine; three months, three; six months, four; ten months two; thirteen months, one; eighteen months, three; two years, three; four years, three; five years, one; from six to seven years, one; ten years, one; fourteen years, one, and more than twenty years, one (osteomyelitis).

8. Sebestyén has written a long paper on trauma in connection with bone sarcoma, *Arch. f. klin. Chir.* 136:4, 1925. He believes that there can be no question that trauma is a causative factor in bone sarcoma.

The influence of trauma in sarcoma of the bone has been discussed further by one of us (W. C. B.) in another article (Internat. J. Surg. 39: 259 [July]; 318 [Aug.] 1926).

EXPLORATORY OPERATION

During recent years there has been a tendency to emphasize the dangers of exploratory operation in tumors in general, particularly in tumors of the long bones, with the result that many surgeons have discontinued this practice. We believe that the dangers have been greatly overestimated. While it is true that in a number of cases the clinical and roentgen-ray findings are sufficiently clear to establish a definite diagnosis, on the other hand, there are certain cases, particularly those in the early stages of the disease when proper treatment is most likely to be of avail, in which it is extremely important to make an accurate diagnosis before it is possible to do so by the clinical and roentgen-ray evidence alone. In such cases, we believe exploratory operation is of great value and is attended with comparatively little risk. These cases will be found chiefly in the periosteal group; the tumors are not extremely vascular and the exploratory incision practically always heals by primary union with little or no risk of infection. In the central group, exploratory operation is usually and should be always associated with complete curettage, thereby greatly increasing the chances of controlling the growth by subsequent toxin and radium treatment after curettage.

Littlewood⁹ of Leeds, England, emphasizes the importance of exploratory operation in long bone sarcoma. As he states,

So often we wait to see if the condition is inflammatory when an exploratory operation would clear up the doubt. During recent years, I have explored four cases of enlargement about the lower end of the femur, thinking they might be sarcoma and then found them to be traumatic periostitis associated with some myositis ossificans.

We have recently had a similar case at the Hospital for Ruptured and Crippled. This patient, a man, with an indefinite history of injury, was transferred to our service from the orthopedic department. There was a tumor of the femur of about seven months' duration, not associated with any temperature or other signs of inflammation. Roentgen-ray examination showed an apparent osteogenic periosteal sarcoma with considerable new bone formation. Exploration, however, revealed in addition to the new bone formation a considerable quantity of purulent fluid, which bacteriologic examination showed to be caused by *Staphylococcus aureus* infection. Exploratory operation in this case was the best possible form of treatment, for had we used roentgen rays,

9. Littlewood, H.: Amputation at the Shoulder Joint for Humerus, Brit. J. Surg. 1: 381 (March 11) 1922.

radium or toxins for a considerable period, until the diagnosis had been established, the infection in the meantime would have caused greater destruction of the femur (case 35).

The opposition to exploratory operation in sarcoma of the long bones is based on two assumptions: (1) the danger of serious infection following the operation, and (2) the danger of generalization of the disease. While there undoubtedly are a few cases in which infection has followed exploratory operation and necessitated amputating the limb in order to save the life of the patient, these cases, we believe, have practically all occurred in the central group, and before the introduction of the surgical solution of chlorinated soda (Dakin's solution).

If we are dealing with a central sarcoma or a giant and spindle cell sarcoma, simple exploratory operation should never be performed, but rather should be an important part of the treatment itself; that is, as much of the tumor as possible should be removed with a curet and the cavity swabbed out with chloride of zinc or phenol. As soon as possible thereafter, the patient should be put on the mixed toxins of erysipelas and *Bacillus prodigiosus*, supplemented if possible with either radium or roentgen rays. Our experience shows that patients treated in this way have better results and show more prompt recovery of function than those treated with roentgen rays or radium alone.

In the present article, however, we are chiefly concerned with periosteal sarcoma. Exploratory operation in these cases is nearly always followed by primary wound healing with scarcely ever any infection. In a few cases of central malignant or telangiectatic sarcoma the wound may fail to heal promptly and may become the site of a rapidly growing fungating tumor, later necessitating amputation. Amputation should be performed as soon as the diagnosis is made and not after prolonged treatment. As to the second danger of producing generalization of the disease by the exploratory operation, we believe the risk almost entirely theoretical. The fact that an exploratory operation was performed in nearly all our cases in which the patient was cured shows that in these cases at least the operation did no harm. We have never seen a case in which there was good reason to believe that the operation hastened the development of metastases.

We have observed a case of chondrosarcoma of the humerus in which exploratory operation showed a tumor of the upper end of the humerus; roentgen-ray treatment was given for a period of five months, during which time the tumor rapidly increased in size and became fungating; finally amputation was performed when the disease had nearly reached the stage of inoperability, and it was necessary to give the patient transfusion before amputating. After the operation, the patient remained well for over a year; but in July, 1925, he developed metastases of the lung, and died a few weeks later. Had the amputation been

performed immediately after the exploratory operation, the chances of a cure would have been much greater.

It is often important to know the type of tumor with which we are dealing in order to advise the method of treatment most likely to effect a cure or the greatest amount of alleviation. In the typical case of sarcoma of the long bones, the clinical history and roentgenograms will enable one to make a positive diagnosis in a fairly early stage of the disease; and in these cases we would not advise exploratory operation. There are other cases, however, in which we cannot make a positive diagnosis in the early stages without an exploratory operation, and in these cases we regard biopsy as of the greatest possible value. In illustration of this point we would cite cases 13, 23 and 35.

In a doubtful case in which it is impossible from the clinical and roentgen-ray data to determine whether the condition is one of osteomyelitis, myositis ossificans or sarcoma, shall we go on with the roentgen ray or radium treatment until the clinical and roentgen-ray signs make the diagnosis clear? Our experience shows that by following this course, not infrequently metastasis of the lung or generalization of the disease occurs before it is possible to establish the diagnosis, even though distinct local improvement may be taking place. On the other hand, is there any sound reason why we should not perform a comparatively safe exploratory operation, at once gaining thereby the valuable information which the exploratory incision and a microscopic study of the sections afford?

As stated before, the danger of infection following exploratory operation in periosteal sarcoma should be comparatively nil for the reason that should the microscopic examination show the tumor to be an osteogenic sarcoma with much new bone formation, then immediate amputation should be performed, followed by the use of the toxins. In this case, there would be little chance for infection to occur. Furthermore, exploratory operation should never be advocated as a routine practice by any surgeon but it should be performed only by the surgeon who is to take charge of the final treatment of the case. The gross appearance of the bone, as revealed by exploratory operation, will often give as much or more information to the surgeon who has had long experience with bone neoplasms as the microscopic picture itself, and he should have the benefit of both.

From a practical point of view, it would be interesting to know in how many of the more than fifty cases of the present series in which the patients are living an exploratory operation was performed. We find this to have been the method of procedure in twenty-seven of the thirty-five cases in which the patients are well from three to twenty-eight years, showing that exploratory operation in this group did not interfere with the chances of curing the disease.

It must be admitted that there are certain cases in which it is impossible to make a definite diagnosis from the clinical history and roentgenograms even when supplemented by a microscopic examination of the section by a competent pathologist; but these cases are rare exceptions, and should not influence us in our attempt to formulate a general rule.

The fact has often been emphasized by Ewing and others that even with all the modern aids to early diagnosis, an early diagnosis of sarcoma of the long bones, or of bone sarcoma in general, is seldom made even by experienced surgeons. While we may agree that in the majority of cases of bone sarcoma, a correct diagnosis can be reached from a careful clinical history and the roentgen-ray findings, this can only be done by one who has had much experience in this disease. One of the great difficulties lies in the fact that the average surgeon sees but a few during many years of practice, and never a sufficient number to enable him to become familiar with the many types of the disease.

METHODS OF USING RADIUM

Up to 1916 when radium was first used in the treatment of sarcoma of the long bones at the Memorial Hospital, the supply was very limited. It was used in the form of a small plaque with silver and lead filtration; this was placed near the surface of the skin, not more than 0.5 cm. distance from it. Superficial burns resulted from this method of application, and little effect was noticed on the tumor, with the exception of one case. In 1916, when the Memorial Hospital received a gift of a large amount of radium, we began to use it in the form of a pack containing from 1 to 2 Gm. filtered by 0.5 mm. of silver, and 2 mm. of lead, later changed to brass, and placed from 6 to 10 cm. from the skin. From time to time the dose has been varied. In the earlier cases we ordinarily gave from 10,000 to 20,000 millicurie hours at 10 cm. distance at a single treatment, repeating this from four to six weeks later. In a case of sarcoma of the femur, as high as 50,000 millicurie hours divided over three areas, anterior, posterior and lateral, about 17,000 millicurie hours over each, have been given as a single treatment covering a period of three to four days. This patient developed extensive generalization of the disease within two months.

In 1917, we began using bare tubes of unfiltered radium inserted through a hollow needle into the depths of the tumor. At first the dose was limited to from 10 to 25 millicurie hours; but during the last year, as high as 78 millicurie hours of unfiltered radium in bare tubes was used in a case of periosteal sarcoma of the shaft of the femur. This large dose had a very slight and only very temporary retarding effect on the tumor; in spite of additional very heavy radiation given in the form of a pack, the disease continued to progress, causing death about two

months later. In several other cases, a combination of bare tubes and radium-pack treatment was employed.

The largest amount of radium in the form of a pack thus far used by us at the Memorial Hospital was 150,000 millicurie hours spread over a period of nearly two years. In this case, a giant cell sarcoma of the femur, the patient made a complete recovery and is still well five years later. While in this case no burn followed the use of the radium, the joint became practically ankylosed, the skin became bronzed and of a leathery texture, and the bone was apparently rendered more brittle, as two years later following a slight injury a fracture occurred just above the site of the previous tumor of the femur. It is interesting to note that in this case union was very much delayed, and the patient's disability extended for more than a year. Undoubtedly, too large a dose of radium had been used. In another case, a periosteal sarcoma of the femur, in which a large amount of radium and roentgen rays was used, the lower part of the femur just above the site of the tumor became so markedly sclerosed that a fracture occurred while the patient was lying in bed. The disease was not controlled even by this large amount of radium. In a case of periosteal sarcoma of the femur, 209,000 millicurie hours were used in the short space of two months by one of our colleagues; the lesion was not controlled.

We do not believe it is possible at the present time accurately to estimate the exact amount of radium or roentgen rays the skin is able to stand without being seriously damaged or without causing serious endarteritis of the deeper vessels. In view of the fact that very serious results may follow the use of too large amounts of radium or roentgen rays, we believe it is most important to keep within the safe limits.

At present we have no evidence to prove that the introduction of bare tubes in bone sarcomas produces any better results than the application of external radiation in the form of a pack. Recently, gold plated bare tubes have been used at the Memorial Hospital with marked benefit in tumors of other parts of the body, particularly the tongue; the gold plate shuts off many of the beta rays and permits the use of a larger dose without causing sloughing or destruction of tissue. It is possible that this method may offer some advantages over the ones previously tried.

The only cases of periosteal sarcoma that we have been able to find in the literature in which the tumors have disappeared under radiation and the patients have remained well five years are the three cases reported by Dr. A. E. Hayward Pinch, medical superintendent of the Radium Institute of London. Jan. 6, 1926, he stated:

My two cases of periosteal sarcoma are still alive; one was treated in June, 1913, and the other in February, 1914. The nature of the disease had been veri-

10. Pinch, A. E. H.: Personal communication to the authors.

fied in each case by microscopical examination before the radium treatment was given, and reported as definite periosteal sarcoma. Incidentally, I heard of a third case six months ago, a lad whom I treated in 1911 for periosteal sarcoma of the thigh. He is now a captain in his majesty's army and in perfect health. As regards osteogenetic sarcoma, I have no good cases to report; this type of disease seems nonamenable to effective radium treatment.

In our opinion, the cases (reported) by Dr. Pinch must have been of the round cell or endothelial (endothelioma, according to Ewing) type, and not osteogenic sarcoma. Pinch's cases were all treated by the introduction of silver tubes into the tumor, which were then removed.

EFFECTS OF PROLONGED IRRADIATION

We are just beginning to appreciate some of the disadvantages and dangers of prolonged radiation, especially in cases of bone tumors. These results show how far we are at present from an understanding of the most efficient and, at the same time, safe dose of radium or roentgen rays. In the great majority of cases of periosteal sarcoma of the long bones, death has occurred before there has been an opportunity of observing the later effects of prolonged radiation; but we have had a few patients who survived sufficiently long to show certain important pathologic changes. In several cases marked changes in bone have taken place; i. e., the bone has been transformed into a hard, ivory-like tissue, exceedingly brittle, and prone to fracture under little or no strain.

In some of our cases the limb has been amputated, thus affording an opportunity for a careful macroscopic and microscopic study. In some instances we have found the marrow cavity almost completely obliterated or transformed into an ivory-like tissue, exceedingly brittle; in the event of a pathologic fracture this bone, by reason of the obliteration of the blood vessels, has shown little power to form new callus or to initiate the normal process of repair. In addition to the changes in the bone, we have found marked changes in the soft parts consisting of general endarteritis, complete occlusion of many of the smaller vessels, with marked fibrosis and transformation into a leathery tissue. In some cases, these changes brought about by overradiation are accompanied by severe pain. In one case of giant cell sarcoma of the femur, a small area of ulceration about three-fourths inch (1.8 cm.) in diameter developed two years after treatment, accompanied by severe pain. Whether the pain was due to the ulceration or to the general endarteritis, it was impossible to say; but it became so severe that amputation had to be performed about eight months later. Although the amputation was done about 6 inches (15.2 cm.) above the area of maximum radiation, the soft tissues over the stump recently became greatly thickened and extremely painful so that it was necessary to perform a second operation for the removal of this abnormal tissue, which was about 1 inch

(2.5 cm.) in thickness and so hard that it was almost impossible to cut it with a knife. In another case, referred to by one of us¹¹ and reported in full by Bancroft,¹² the patient was treated with roentgen rays following curettage for a small benign giant cell tumor of the radius. Although the disease was cured, the resultant pain and osteomyelitis of the bone from overirradiation made it necessary to resect the radius and ulna (fourth operation performed), leaving a much impaired hand.

These results are sufficient to show that when using radium or roentgen rays in bone cases, careful thought should be given to the dosage, and the danger of overirradiation should be appreciated. At a recent conference at the Memorial Hospital, one of the visitors in discussing these cases stated that we should not be concerned if we did devitalize or destroy a large portion of the long bones (tibia or femur) because we can then amputate, and that preoperative radiation would prove an important factor in preventing metastases. As we have already stated, we believe that at present there is not the slightest evidence in support of this view. We have no evidence that radium or roentgen rays, even when carried to the point of devitalizing the bone, has ever succeeded in entirely destroying a primary osteogenic sarcoma of the bone, much less prevented its metastasizing. If no metastases have occurred at the time of the amputation, caused by the escape of tumor cells in the lungs or elsewhere, we can see no advantage in preliminary radiation. If some of these tumor cells have escaped before radium treatment is started, then no amount of prolonged radiation of the tumor of the long bone will have material effect on metastases already present.

PREOPERATIVE IRRADIATION IN BONE SARCOMA

We have never been convinced of the wisdom or value of radium or roentgen rays as a preoperative measure in any type of cancer, and we believe that at present there is no definite evidence of the value of either agent as such a measure. While preoperative radiation has been strongly advocated by many roentgenologists, and a number of surgeons have adopted it as a routine measure, Greenough¹³ of Boston in a paper read before the American Cancer Research Society in 1923 stated that there is no proof of its value in cancer of the breast and that it was attended by certain distinct disadvantages in the way of delayed wound healing. Also, Wood¹⁴ of New York has come out strongly against preoperative radiation in cancer in general. Lee¹⁵ believes that preoperative radia-

11. Coley, W. B.: Prognosis in Giant Cell Sarcoma of the Long Bones, *Ann. Surg.* 79:321 (March); 561 (April) 1924.

12. Bancroft: *S. Clin. N. Amer.* 1:1739 (Dec.) 1921.

13. Greenough: Cancer of Breast, *Tr. Am. Cancer Research Society*, 1923.

14. Wood, F. C.: *S. Clin. N. Am.* 5:263 (Feb.) 1925.

15. Lee, B. J., and Herenden, R. E.: *Ann. Surg.* 82:404 (Sept.) 1925.

tion is of distinct advantage in cancer of the breast. We believe that the question is still subjudice as regards malignant tumors in general, but in the special field of long bone sarcoma in the cases in which it has been definitely decided that early amputation offers the greatest hope of saving the life of the patient, we can see no advantage in preoperative radiation. In these cases the use of this measure can be justified only on the ground that the action of radium or roentgen rays on the tumor cells produces certain changes in the body fluids which may have an inhibitory action on the tumor cells that have already escaped from the primary tumor through the circulation or lymphatics and have been carried to other parts of the body, later giving rise to metastatic tumors. Such action is not yet proved. In a number of our cases the evidence certainly points to the possibility of metastases being directly brought about by heavy radiation, and we can see no ground for taking the risk of such a result, especially in cases in which from the start we believe there is no reasonable hope of controlling the disease or of saving the limb by radiation. In these cases, it would seem far wiser to perform an immediate amputation following this with prophylactic toxin treatment supplemented by roentgen-ray treatment over the chest.

We are aware that some observers, in fact, two of our own colleagues at the Memorial Hospital, believe that preliminary radium or roentgen-ray treatment may be of decided value in long bone sarcoma even if the case goes on to amputation. This belief is based on the theory that certain changes may be produced by the roentgen rays or radium that may lessen the chances of metastases after amputation. Whatever may be the theoretical grounds for this belief, it is evident that the question can be settled only by actual experience, and fortunately we now have a sufficiently large number of cases treated by preliminary radiation followed by amputation to permit some definite conclusions (for example, case 109 in table 7).

We have a group of twenty-four cases in which either the roentgen ray or radium was used for varying periods and amputation then performed after failure to control the disease by radiation; of these sixteen are dead and two others have pulmonary metastases. Only one of these patients has remained well for more than three years; the remaining cases are too recent to enable one to draw any deductions as to the final outcome.

We have another group of twenty-seven operable cases of osteogenic sarcoma in which roentgen rays or radium was given as a primary method of treatment in preference to early amputation, in which either metastases developed or the condition became inoperable during the course of treatment. If we compare this group of cases with a similar group treated with toxins alone or toxins and radium after amputation we find a striking contrast. These last two groups were practically

identical as regards the pathologic or histologic type of tumor, so that it is quite fair to compare the results of the different methods of treatment.

In spite of our results at the Memorial Hospital, and in spite of the uniformly poor results of other men, we have continued using roentgen rays and radium year after year, in the hope that further experience and increased knowledge as to the best method of applying these agents might result in a cure of this baffling disease. The time has now come, we believe, to pause and reconsider the problem. It might be well to ask ourselves if we are any longer justified in advising a patient with an operable periosteal or osteogenic sarcoma of the long bones to undergo a course of radium or roentgen-ray treatment as a primary measure before amputating, at least without telling him frankly that we can offer no hope of saving his limb, and that later amputation offers little hope of saving his life. If the tumor is of the round cell variety (endothelioma, according to Ewing) in the operable stage or spindle cell with little new bone formation, we could tell the patient that there is a small chance of saving his limb by a combination of toxins and radium treatment, but that if marked improvement is not noted in a few weeks, amputation should be performed, followed by prophylactic toxin treatment, and that this measure offers a practically even chance of saving his life. If the patient prefers to lose his life rather than his limb, then, and then only, are we justified in the use of prolonged radiation alone in the osteogenic type.

The following question naturally arises: Have we as yet sufficient evidence as to what can be accomplished by radium and roentgen rays in osteogenic sarcoma to enable us to decide whether radiation should be the method of choice in early primary cases? While the question cannot be regarded as definitely answered, it would seem that our own failure to produce a single cure of undoubted osteogenic sarcoma in which the diagnosis was established by microscopic examination, and the fact that the observations of distinguished radiologists here and abroad are in entire accord with our own, justifies us in reconsidering the whole question. Regaud, director of the Radium Institute of Paris, Forschell of Stockholm, Pinch, director of the Radium Institute of London, and Burnham of Baltimore, all agree that bone sarcoma is exceedingly resistant to roentgen-ray or radium treatment, and no one has reported a cure in osteogenic sarcoma. In his annual report for 1921, Pinch stated:

It is to be noted that radium treatment is useless in all cases of disease affecting actual bone substance, whether malignant or nonmalignant. It has been tried in such widely diverse conditions as rodent ulcer affecting the cranial bones, osteosarcoma, myositis ossificans, osteitis deformans and ivory exostosis, and in no instance has the least benefit ever been recorded.

We believe that our own results further warrant us in abandoning radiation as a routine method of treatment in early primary osteogenic sarcoma, and substituting early amputation followed by prolonged toxin treatment systemically, and postoperative radiation to the lungs.

Dr. Pinch has stated:

In my experience, radium is useless in cases of endosteal sarcomas of the osteogenic type, and I have never succeeded in effecting the slightest improvement in this class of disease.

AMPUTATION

A fairly accurate idea of the curative value of radical operation alone (amputation or extirpation) in sarcoma of the long bones may be obtained from a study of the statistics of the Tübingen Clinic (Professor von Bruns) reported by O. Kocher; these statistics have already been quoted in full in our earlier papers on the subject. The latest and most authoritative statistics showing the results of radical operation alone in sarcoma of the long bones may be found in an article by Escher¹⁶ covering sixty-three cases treated at the von Eiselberg Clinic, Vienna, from 1901 to 1918. Of this series twenty-one patients died of metastases, and nineteen without metastases, within one year of the operation; thirteen were of periosteal origin and twenty-three were myelogenous; only six of the sixty-three patients were reported well beyond a two-year period. In twelve cases resection was performed, and in the remainder, amputation. Among the cases apparently cured by amputation were: (1) a chondrosarcoma of the tibia of five years' duration before amputation, well eight and one-half years; (2) a chondrosarcoma of the femur of four years' duration, well eight years after hip joint amputation; (3) a periosteal round cell sarcoma of the lower end of the humerus, well eighteen years after amputation at the shoulder joint.

Escher discusses the various methods of conservative treatment only to discard them all, and places himself on record as being in favor of nothing less than immediate radical amputation, a resection, in both the periosteal and myelogenous types of sarcoma of the long bones. He adds that, in spite of the great progress in roentgen-ray therapy, such treatment does not result in an actual cure in cases of bone sarcoma, although it may be of great value in inoperable cases. Resection he regards of value only in the early stages in which the tumor is undoubtedly encapsulated. A striking fact brought out by the statistics of these two clinics is that the malignancy of the central or myelogenous group of sarcomas very nearly equalled that of the periosteal, and this is true of Kocher's series.

16. Escher: *Arch. f. klin. Chir.* 114:553, 1920.

Our own series of cases show that amputation alone, even when performed at an early stage of the disease, rarely results in a cure. A recurrence or metastasis has taken place within from a few months to a year in 98 per cent of the cases. We have no patient treated by amputation alone, without preoperative toxin or radium treatment, who has remained alive and well for a period of three years. Our series show only twelve patients treated by amputation alone, with no cures. According to Bloodgood, only two out of his seventy patients with periosteal sarcoma treated by amputation survived the three year period.

At a symposium on long bone sarcoma held during the meeting of the American College of Surgeons in Philadelphia in 1922, Meyerding of the Mayo Clinic reported the end-results in 100 cases of sarcoma of the long bones treated at the Mayo Clinic since 1910 (with complete roentgen-ray, clinical and pathologic data). In many of these cases, amputation had been performed, followed by a routine course of toxin treatment, in some cases supplemented by roentgen rays. A careful follow-up showed 50 per cent of the patients still alive, 16 per cent well over five years. In striking contrast to this was the report of Besley of Chicago, who took part in the discussion at the same meeting. He stated that of fifty-six cases of sarcoma of the long bones treated by amputation at the Cook County Hospital, in which no prophylactic treatment had been given, not a single patient operated on prior to September, 1920, was known to be alive at the time of his report, irrespective of the pathology of the tumor.

Thus far the periosteal cases have been grouped without regard to the histologic type. While the end-result is death in practically all the cases regardless of the type of cell, the duration of life varies considerably in the different histologic types. In the round cell variety, classified by Ewing as endothelioma, death often occurs within from six months to one year, while in the sclerosing or osteoid type the duration of life may be two years or more. The duration of the disease is likewise materially altered by the method of treatment employed. In many cases the disease has been held in check for months, and in some cases for two or three years, by roentgen rays or radium; unfortunately, however, these cases have gone on to a fatal issue. As a rule, the cases in which there is little or no new bone formation (round cell sarcoma or endothelioma) show the greatest effect from both roentgen rays and radium, in some cases amounting to practically complete disappearance of the tumor as far as clinical and roentgen-ray evidence goes; yet in nearly all of these cases recurrence of metastases develops, usually within from a few months to a year. The cases characterized by marked new bone formation—the ordinary type of osteogenic sarcoma—show extreme resistance to roentgen rays, radium or toxins, and while some temporary improvement is often observed, it is usually only of short duration. In a number

of these cases, metastases have developed during the early stages of roentgen-ray or radium treatment, whether favored by the rapid breaking down of the tumor, thus permitting living cells to be carried to remote parts of the body, or merely as a coincidence, it is impossible to say. We have observed a number of cases that would seem to suggest the possibility of metastases having been caused or hastened by treatment.

Whether this is true or not, the fact remains that no patient with this type, that is, with marked new bone formation, has been cured by roentgen rays or radium or toxins. Therefore, we can see no reason why any of these methods of treatment should be employed in this type of tumor unless it can be shown that no other treatment offers any greater hope of saving the life of the patient. This brings us to a consideration of the other alternative: amputation followed by prolonged treatment with the mixed toxins of erysipelas and *Bacillus prodigiosus*. Fortunately, we have a fairly large group of cases including many of the type just mentioned that have been treated by amputation followed by the use of the toxins. Of the group of forty-one cases so treated, twenty, or 49 per cent, have remained well from three to eighteen years. In three of these cases the toxins were given for less than two weeks, too short a period in which to expect much benefit. The importance of these results is at once apparent when we compare them with the smaller group of patients treated by amputation alone (no cures) or amputation after prolonged radiation (only one patient, well three years). If amputation had been performed earlier in many of these cases and had been followed by toxins, we believe that an even larger number than 50 per cent might have been saved.

In view of these results, we feel justified in urging immediate primary amputation in all cases of osteogenic sarcoma associated with a large amount of new bone formation, to be followed by prolonged toxin treatment. Conservative treatment of any kind is not justified in this group of cases for the reason that the time intervening, necessary for carrying out the conservative treatment, materially increases the chances for the development of metastases, whether or not such development is favored by the action of the treatment. If there were any hope of a cure of the patient by such treatment, there might be some justification for attempting to save the limb, but thus far we have no evidence encouraging us in this hope.

INOPERABLE CASES

It has been found possible to save the life as well as the limb in a limited number of inoperable cases, in which the disease had advanced too far for amputation at the time of first observation. These cases are of sufficient interest to warrant a brief reference: We have ten cases

(cases 3, 4, 15, 19, 21 and 22) in which the disease had advanced beyond any hope of relief from surgical measures which have been successfully treated, and the patients have remained alive and well from two to twenty-four years. In at least one case, definite lung metastases were present at the time the treatment was begun, and in four other cases there was evidence of probable metastases. A further study of these cases shows that none was of the periosteal osteogenic type with a large amount of new bone formation, but rather of the round cell sarcoma type, or, according to Ewing's recent classification, endothelioma, a type that has been found to respond much more rapidly to toxins, roentgen rays and radium than the osteogenic type.

In one case, an extensive sarcoma of the tibia with metastases in the inguinal and iliac glands, the tumor was pronounced osteogenic sarcoma by Ewing, but the roentgenogram showed no marked new bone formation. This patient recovered under radium and prolonged toxin treatment, his limb was saved, and he is in good health, nine years later.

ENDOTHELIOMA

Of the twenty-six patients with endothelioma, as well as round cell sarcoma without new bone formation, included in this series of cases, thirteen are alive and well from three to fifteen years. It is interesting to note the method of treatment employed in these living patients:

1. Tibia; radium for from two to three years followed by amputation; well, one and one-half years; Ewing's diagnosis.
2. Femur; amputation for sarcoma of femur; was then treated with toxins and radium for multiple metastases in skull; well six years later; Ewing's diagnosis.
3. Fibula; amputation; multiple metastases developed in groin, iliac fossa and lungs; treated with toxins and radium; patient well five years later; Ewing's diagnosis.
4. Femur, extensive involvement; amputation followed by toxins; patient well fifteen years later; Ewing's diagnosis.
5. Femur; extensive metastases to pectoral region and ilium; roentgen-ray treatment to femur; metastases of ilium treated with toxins alone; patient well ten years later; diagnosis by Dr. E. K. Dunham, professor of pathology, Bellevue Hospital Medical College.
6. Femur; diagnosis from clinical and roentgen-ray evidence and macroscopic examination on exploratory operation; treated with toxins alone; limb saved; patient well ten years later.
7. Femur; inoperable; clinical and roentgen-ray diagnosis; treated with toxins and radium; patient well seven years later.
8. Tibia; amputation followed by toxins; patient well seven years later; microscopic diagnosis confirmed by Ewing.
9. Clavicle; treated with radium alone; patient well three years later; died, July, 1925, cause of death unknown; no local recurrence; Ewing's diagnosis.

10. Clavicle; excision followed by toxins; patient well fifteen and one-half years later; Ewing's diagnosis.

11. Tibia; clinical and roentgen-ray diagnosis; treated with toxins and radium; limb saved; patient well five years later.

12. Femur; treated with toxins and radium; limb saved; patient well five years later.

13. Clavicle; clinical and microscopic diagnosis; round cell sarcoma; excision followed by toxins; patient well seventeen years later; diagnosis by Dr. W. F. Whitney, Harvard Medical School.

In September, 1905, Howard and Crile¹⁷ of Cleveland published an important article on endothelial bone tumors containing a report of nineteen cases found in the literature in addition to four cases that had come under their personal observation. The locality of the tumor in the nineteen cases was: the humerus in seven, the tibia in three, the femur in eight, and the ulna in one case. In the majority of these cases the origin of the tumor was apparently in the central portion of the bone from which it spread along the narrow cavity and later involved the entire bone. The tumors were quite vascular and, in several cases, were mistaken for bone aneurysm. In 63 or 64 per cent metastases were observed. We find few references in the medical literature to endothelioma of the bone until Ewing¹⁸ in 1921 reported a most interesting case which he classified as endothelial myeloma and which probably belonged to the same group of tumors. Since that time there have been observed at the Memorial Hospital sixteen cases of malignant tumors of the long bones, practically all of which occurred in the shaft of the bone, which have been classified by Ewing as endothelioma or endothelial myeloma. While most of these tumors are still classified by the majority of pathologists as round cell sarcoma, and while there may be good reasons for hesitating to accept the view that they are of endothelial origin, we must admit that they do form a fairly definite clinical and pathologic group and differ materially from the ordinary type of osteogenic sarcoma. Furthermore, they differ quite as much in their response to treatment with radium, roentgen rays or toxins.

The clinical features of a typical case are somewhat as follows: The trouble usually originates in the shaft of a long bone instead of in the neighborhood of one of the ends of the bone, which is usually the case in osteogenic sarcoma. There is a history of antecedent local trauma in about the same proportion of cases as in the ordinary type of sarcoma. The tumor is apt to involve a considerable portion of the bone, one half to one third of the shaft, at the time of first observation. While the trouble usually starts in the central portion of the bone, there are cases

17. Howard and Crile: *Ann. Surg.*, September, 1905.

18. Ewing, James: *Rep. New York Path. Soc.*, 1921.

in which it apparently originates in the periosteum or subperiosteal tissue. It seldom destroys sufficient bone to cause a pathologic fracture, although pathologic fracture has been observed in several of our own cases. It shows little or no tendency to produce new bone, and in these cases one never sees the marked new bone production with typical lines radiating at right angles to the shaft of the bone. It has more of a tendency to produce separate layers of tumor tissue laid down parallel to the shaft of the bone. In our own series of cases, the tumors have not as a rule proved to be so highly vascular as has been found by Howard and Crile. One of our most recent cases was highly vascular. In contradistinction to the ordinary osteogenic sarcoma these tumors show marked susceptibility to the influence of roentgen rays, radium and toxins, often disappearing entirely after a few weeks' treatment; unfortunately, however, the disease is apt to recur within a few months either locally or in the form of metastases to the lungs or other bones. This type of tumor shows a special predilection to invade other bones, especially the skull.

These cases have been generally described as round cell sarcoma by most pathologists. They resemble round cell sarcoma in that they are composed of diffusely growing cells with round nuclei. Ewing states that three anatomic forms may be recognized: (1) multiple endothelioma; (2) solitary angio-endothelioma and (3) diffuse endothelioma. Ewing cites Marckwald's case of multiple endothelioma in which nearly every bone in the body was the seat of small medullary tumors; he states that this is the only recorded case of its kind, although Symmers and Vance¹⁹ describe a somewhat similar one. While in several of the cases compiled by Howard and Crile multiple tumors were observed, these were regarded as secondary. These authors state that this type of tumor is more prone to produce metastases than any other, 66 per cent of their cases having metastasized. Whether the tumors in this group were primary or secondary and metastatic from one original growth, Ewing believes it is impossible to determine. A study of our own cases strongly supports the opinion that the multiple tumors that practically always develop a considerable period of time after the original tumor are really metastatic. He states: "The structure consists of endothelial-like cells in small groups or sheets, often forming alveoli and sometimes cysts containing serous or mucinous fluid."

ANGIO-ENDOTHELIOMA

According to Ewing, this form "usually appears as a single tumor which sharply and completely destroys the bone and often reaches large dimensions. Its expansile pulsation places it among the malignant bone aneurysms. The roentgen ray shows a clean cut destruction of bone by

19. Symmers and Vance: *Am. J. M. Sc.* 152:28 (July) 1916.

The question of the best method of treatment of this type of tumor primary in a long bone is still a difficult one. While Ewing in his publication of 1922 pointed out the fact that these tumors were remarkably susceptible to roentgen rays and radium and that, therefore, amputation was probably unnecessary, up to that time he was unable to report a single cure of this type by radiation and stated that "it does not appear that any cases have been treated by modern roentgen-ray technique." He believes the diagnosis can generally be made on the clinical history, the peculiar roentgenogram, and the early response to radium. He adds, however, that competent observers have firmly maintained that some of his cases were osteomyelitis. Since 1922 there have come under our observation three other cases in which the clinical and roentgen-ray evidence, as well as the microscopic examination following exploration, all pointed to a diagnosis of osteomyelitis, and yet the subsequent history proved them to be endothelial type sarcoma. We ourselves feel that the advantages to be gained by an early diagnosis in doubtful cases greatly outweigh the disadvantages of exploratory operation.

TABLE 3.—*Age of Patients in Endothelioma Group*

| | Patients |
|----------------------------------|----------|
| Up to and including 5 years..... | 2 |
| 6 to 10 years..... | 6 |
| 11 to 20 years..... | 7 |
| 21 to 30 years..... | 5 |
| 31 to 40 years..... | 5 |
| 41 to 50 years..... | 1 |
| Sex: 17 males, 9 females. | 26 |

Since Ewing's paper was written (1922) we have had an opportunity of studying a number of additional cases, making at present a total of twenty-six cases. While this further study has confirmed all that he said about the striking susceptibility of these tumors to roentgen rays and radium, so far we have not succeeded in curing a single case by either of these agents alone. On the other hand, we have succeeded in causing the total disappearance of the tumors in two far advanced cases with multiple metastases (in the skull in one case, and in the inguinal and iliac glands and lungs in the other), and both patients are now in good health, more than five years later, following combined treatment with toxins and radium. These cases are so remarkable that they are given in detail. In another far advanced case the disease was apparently controlled and the patient remained well for nearly two years, when she developed metastases in the abdomen and brain, which proved fatal. If to these cases we add the two previously mentioned, occurring in the early series before the condition was recognized, we have two more patients cured and well more than ten years, treated by toxins and

roentgen rays in one case and toxins alone in the other. The limb was saved in both cases and the patients are well at the present time.

Our own observations force us to believe that the cases that begin with multiple primary tumors must be very rare. We have never observed such a case and we are inclined to regard the subsequent development of multiple tumors as merely a generalization of the disease from a single primary focus.

From a study of our own series of cases, which represented different degrees of malignancy—in certain cases the disease ran a rapid course, killing the patient in a few months, and in other cases, the disease continued for one or two years before proving fatal—we have not found it possible to determine definitely the degree of malignancy by the histologic structure of the tumor.

In regard to the first group mentioned by Ewing, i. e., encapsulated extraperiosteal fibrosarcoma, while these tumors may be less malignant than those mentioned in the other groups, they are extremely rare, and we found only one case of this type in our series. This patient was treated first by local exploratory operation, and later by radium and roentgen rays; at the end of the third year, a pathologic fracture occurred; an amputation was performed one year ago; the patient was well, January, 1926, nearly two years after operation. On the other hand, we have examples of subperiosteal sarcoma diagnosed as fibrosarcoma, in which the disease ran a rapid course, causing death within six or eight months.

There is another group of cases in which surgical opinion varies considerably in regard to the prognosis; this is the so-called chondrosarcoma or osteochondrosarcoma in which there is considerable cartilage in the tumor. Many have regarded these cases as less malignant in that they run a slower course. A study of our own series, as well as the cases reported in the literature, shows that many of these cases run a comparatively rapid course, and that few if any are cured by amputation alone.

There is a rare type of sarcoma designated by Gross as chondro-osteoid sarcoma, and often called the sclerosing type of sarcoma, in which the prognosis as to duration of life is better than in the more cellular types. Practically all of these cases end in death after amputation alone. In some cases the disease may last a number of years, four or five or more, and yet in cases of long duration there is always the possibility that the original trouble may have been a traumatic productive osteitis or myositis ossificans which later on underwent malignant degeneration such as we frequently see in tumors of the soft parts, for example, carcinoma of the breast originating in a chronic mastitis. As a rule the *more highly cellular* the structure of the tumor, the more rapid the growth with the greater probability of early metastases. On the other hand, we have seen a typical fibrosarcoma of the soft parts, so slightly cellular that the pathologist thought it might well be called a fibroma,

develop with great rapidity and cause death from metastases within six months. In one of our bone cases, a tumor of the humerus with extensive involvement of the midshaft, a biopsy was made and Ewing's diagnosis was fibrochondroma of slight malignancy. Several radium treatments were given with little effect; one of us later did an amputation at the shoulder joint, following this by a brief course of prophylactic toxin treatment; metastases developed in four months, causing death a few months later.

These cases show that it is not always possible to determine the degree of malignancy of a tumor of the long bones by the histologic structure.

We believe that our results warrant us in using radium or roentgen rays, preferably the former, in most cases of diffuse endothelioma or round cell sarcoma associated with little or no new bone formation. We believe that by combining toxins with radium in these cases better results are obtained. The fact that we have been able fully to control the disease in several far advanced cases of this type which had already metastasized by the combined treatment with radium and toxins justifies us in the hope that similar treatment in early operable cases may result in saving the limb as well as the life of the patient.

We believe that the use of radium or roentgen rays is still justified in cases of early operable giant cell sarcoma and that it will prove curative in a certain number of cases. That it will prove superior to curettage alone, or curettage followed by toxin and radium treatment (our own choice) is still a matter of grave doubt. It is important to note that our present series of cases shows that the period of treatment with radium or roentgen rays is often greatly prolonged, in some cases over one or two years; that recurrences are not infrequently noted, and that the period of disability is likely to be considerably greater than when surgery-curettage-toxins is the method of choice.

RESULTS OF ROENTGEN RAY AND RADIUM TREATMENT IN PRESENT SERIES OF CASES

Of sixty-seven operable cases of periosteal sarcoma of the long bones, including endothelioma, in which roentgen rays or radium was the primary method of treatment, thirty-six patients are known to have died. As regards the seventeen living patients, in ten amputation or resection was performed and in addition the roentgen ray or radium was used. In the remaining seven living patients, the diagnosis was confirmed by microscopic examination in only one case (sarcoma of clavicle) and in the others in only one case was the clinical and roentgen-ray evidence sufficiently clear to establish the diagnosis beyond reasonable doubt.

A brief résumé of the less recent living cases is as follows:

Case 33; sarcoma of femur; disease was held in check for three years; pathologic fracture occurred; amputation performed; patient well nearly two years later.

Case 13; sarcoma of humerus; roentgen-ray treatment; resection; patient well seven years later.

TABLE 4.—*Primary Operable Cases of Periosteal Osteogenic Sarcoma, Endothelioma and Malignant Central Sarcoma Treated Primarily with Roentgen Rays and Radium, and Later by Amputation After Failure to Control Disease*

| Case | Locality | Treatment | Results |
|------|--|--|----------------------------------|
| 1 | Ulna..... | Radium four months; amputation..... | Death; metastases six months |
| 2 | Humerus..... | Radium six months; amputation..... | Death; metastases five months |
| 3 | Femur..... | Radium | Death |
| 4 | Femur..... | Radium and roentgen rays, 1919; disease controlled four years; pathologic fracture, necessitating amputation | Patient well one year |
| 5 | Femur..... | Radium and high voltage roentgen rays one year; partial control; amputation | Patient well two years |
| 6 | Humerus, periosteal not osteogenic | Radium four months; disease not controlled; amputation | Patient well three years |
| 7 | Tibia, central, giant and spindle cell | Radium; amputation | Death |
| 8 | Tibia..... | Curettage; radium; recurrence; amputation | Death; metastases four months |
| 9 | Tibia, central, giant cell | Curettage; radium; recurrence; amputation | Death |
| 10 | Scapula..... | Radium (tumor disappeared) recurrence; amputation | Death |
| 11 | Tibia, central, giant cell, angio-endothelioma (?) | Roentgen rays; amputation..... | Well one and three-fourths years |
| 12 | Femur..... | Radium; amputation | Death; metastases |
| 13 | Humerus..... | Roentgen rays; amputation..... | Death; metastases |
| 14 | Humerus..... | Roentgen rays; amputation..... | Well two years plus |
| 15 | Tibia..... | Roentgen rays; amputation..... | Death; metastases |
| 16 | Tibia; endothelioma | Radium two years; amputation..... | Well one and one-fourth years |
| 17 | Femur; central, giant cell (clinical and roentgen-ray diagnosis) | Radium and roentgen rays; amputation | Death; metastases |
| 18 | Femur..... | Roentgen rays two and one-half months; amputation | Death; metastases |
| 19 | Femur..... | Roentgen rays six weeks; amputation... | Death; metastases |
| 20 | Tibia..... | Roentgen rays; amputation..... | Death; metastases |
| 21 | Humerus..... | Radium; amputation | Death; metastases |
| 22 | Femur..... | Radium; amputation | Death; metastases |
| 23 | Tibia..... | Roentgen rays; amputation..... | Death; metastases |
| 24 | Os calcis..... | Roentgen rays; amputation..... | Death; metastases |
| 25 | Tibia..... | Roentgen rays; amputation..... | Death; metastases |
| 26 | Femur..... | Roentgen rays six weeks; amputation; toxins six months | Well two years |
| 27 | Tibia..... | Roentgen rays six weeks; amputation | Death; metastases four months |
| 28 | Tibia..... | Roentgen rays four months; amputation | Recent cure |
| 29 | Femur..... | Roentgen rays; amputation..... | Metastases |

Case 28; sarcoma of lower end of humerus; radium treatment for four months; disease not controlled; amputation performed; patient was reported well nearly three years later, but no medical examination was made.

Sarcoma of humerus; resection followed by prophylactic radium treatment; patient well five years later.

Case 12; tumor of femur; roentgen-ray diagnosis; periosteal sarcoma (no microscopic examination); clinical history suggested possibility of myositis ossificans; treated with roentgen rays and radium; well three and one-half years.

Case 34; sarcoma of femur; clinical and roentgen-ray diagnosis (no microscopic examination); treated with roentgen rays; well two and one-half years later.

Sarcoma of clavicle involving the cervical spine; microscopic diagnosis: endothelial myeloma; treated with radium alone; patient in good health for four years; died after a week's illness in June, 1925; cause of death not definitely known.

TABLE 5.—*Operable Cases of Periosteal Osteogenic Sarcoma or Endothelioma Treated Primarily with Roentgen Rays or Radium, which Became Inoperable or Developed Lung Metastases During Treatment*

| | |
|---|-----------------------------|
| 1..... | Clavicle |
| 2..... | Humerus |
| 3..... | Humerus |
| 4..... | Femur |
| 5..... | Humerus |
| 6..... | Tibia |
| 7..... | Femur |
| 8..... | Femur |
| 9..... | Radius |
| 10..... | Femur |
| 11..... | Femur |
| 12..... | Femur |
| 13..... | Femur |
| 14..... | Femur |
| 15..... | Os calcis |
| 16..... | Humerus |
| 17..... | Femur |
| 18..... | Humerus (Bellevue Hospital) |
| 19..... | Tibia |
| 20..... | Tibia |
| Cases in Which Treatment Was Carried Out at Other Hospitals and in Which Patient Was in an Inoperable Condition on Admission to Memorial Hospital * | |
| 21..... | Humerus |
| 22..... | Femur |
| 23..... | Humerus |
| 24..... | Humerus |
| 25..... | Clavicle |

* In several cases in this group, metastases developed soon after the beginning of heavy treatment with high voltage roentgen rays or radium, thus raising the question of whether the too rapid breaking down of a vascular sarcoma by radiation may not cause some of the living cells to be carried to different parts of the body, particularly the lungs, thus producing metastases earlier than otherwise would have occurred.

In twenty-seven patients treated primarily with roentgen rays or radium, the condition became inoperable before amputation was advised or before the patient had consented to it. In twenty-nine cases, amputation was performed after failure to control the disease by radiation; twenty-one of these patients died, and eight are living. In three of the living patients, the mixed toxins were used as a prophylactic after operation; one patient is well nearly two years, another is well a little over one year, and the other case is recent.

In sixteen cases amputation was performed without the use of previous treatment (toxins, roentgen rays or radium) and without any prophylactic after-treatment. In all of these cases death occurred, in the majority about a year after amputation. In one case metastases of the

lungs developed seven years after amputation, and in another, metastases of the skull five years after amputation.

In twenty-four cases preoperative roentgen-ray or radium treatment had been given but no prophylactic after-treatment of any kind. Of this group fifteen died, and of the remaining nine living patients only one has reached the three year period (this patient was indirectly reported as being well, but no physical examination was made).

It is interesting to compare the foregoing results with those obtained in table 6.

TABLE 6.—*Patients Treated by Amputation Followed by Toxins**

| Case | Locality | Result | Remarks |
|--------------|-------------------|---------------------|---|
| 21 | Tibia..... | Well 4 years..... | Diagnosis confirmed by Ewing |
| 22 | Fibula..... | Well 4½ years..... | Diagnosis confirmed by Ewing |
| 8 | Femur..... | Well 15 years..... | Diagnosis confirmed by Ewing |
| 17 | Femur..... | Well 8 years..... | Diagnosis confirmed by Ewing |
| 10 | Femur..... | Well 19 years..... | Diagnosis confirmed by Ewing |
| 31 | Femur..... | Well 10 years..... | Diagnosis confirmed by Ewing |
| (in table 7) | | | |
| 5 | Femur..... | Well 18 years..... | Diagnosis confirmed by Sondern |
| 23 | Femur..... | Well 5 years..... | Diagnosis confirmed by Ewing |
| 21 | Femur..... | Well 6 years..... | Diagnosis confirmed by Ewing |
| 3 | Metatarsal bone.. | Well 23 years..... | Diagnosis confirmed by New York Hospital Laboratory |
| 16 | Femur..... | Well 8 years..... | Diagnosis confirmed by Ewing |
| 12 | Radius..... | Well 12 years..... | Diagnosis confirmed by Ewing |
| 20 | Tibia..... | Well 7½ years..... | Diagnosis confirmed by Ewing |
| 14 | Metatarsal bone.. | Well 10 years..... | Diagnosis confirmed by Ewing |
| 18 | Femur..... | Well 8½ years..... | Diagnosis confirmed by Ewing |
| | Humerus..... | Well 8 years..... | Diagnosis confirmed by Ewing |
| 11 | Ulna..... | Well 15 years..... | Diagnosis confirmed by Whitney (Harvard Medical School) |
| 6 | Femur..... | Well 18½ years..... | Diagnosis confirmed by Ewing |
| | Clavicle..... | Well 15 years..... | Diagnosis confirmed by Ewing |
| | Clavicle..... | Well 15 years..... | Diagnosis confirmed by Whitney |

* Of forty-one patients treated by amputation followed by prophylactic toxins (thirty-nine patients being treated prior to three years ago) the twenty given here are alive and well from three to twenty-eight years.

RESULTS IN CASES TREATED WITH TOXINS ALONE OR COMBINED WITH SURGERY

Of forty-eight patients treated with toxins alone or toxins combined with surgery, twenty-two are alive and well beyond the three year period; in all of these cases the diagnosis was confirmed by microscopic examination; in three additional living patients (in whom the limb was saved) the diagnosis was based on clinical roentgen-ray evidence, but this was sufficiently clear so as to leave little doubt as to the correctness of the diagnosis. In thirty-eight cases of the periosteal type, nineteen of the patients were well from three to eighteen years.

LIVING PATIENTS

Of eighty-eight patients with operable cases of periosteal osteogenic sarcoma of the long bones, including endothelioma, treated with toxins alone, toxins and radium, or amputation and toxins, forty-seven, or 53.3 per cent, are living: thirty-eight are alive and well from three to

TABLE 7.—Group I: Patients Treated by Toxins or

| Case | Date | Age | Sex* | Locality | Trauma | Clinical Diagnosis | Roentgen-Ray Diagnosis |
|------|----------------------------------|-------|------|---------------------------------|---|---|---------------------------------|
| 1 | January, 1907 | 12 | ♂ | Femur, lower end | Kicked above knee; tumor 1 week later | Periosteal sarcoma | Periosteal sarcoma |
| 2 | September, 1912 | 27 | ♀ | Femur shaft, middle two-thirds | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 3 | April, 1907 | 26 | ♀ | Femur, lower end | Dislocated knee cap and wrenched knee 2 years before | Periosteal sarcoma | Periosteal sarcoma |
| 4 | April, 1909 Williamson's case | Adult | ♂ | Femur, lower end | ?..... | Periosteal sarcoma, unoperable (Dr. W. J. Mayo) | Periosteal sarcoma |
| 5 | June, 1890 | 41 | ♂ | Femur, upper end | None..... | Sarcoma..... | None..... |
| 6 | 1915 | 29 | ♂ | Femur, lower end | Yes; local fracture | Periosteal sarcoma | Periosteal sarcoma |
| 7 | March, 1920 | 19 | ♂ | Femur, lower end | Fall 3 months before | Sarcoma..... | Sarcoma..... |
| 8 | 1911 | 21 | ♀ | Femur, lower end | None..... | Periosteal sarcoma | Osteogenic sarcoma |
| 9 | 1919 | 22 | ♂ | Femur, lower end | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 10 | 1917 | 14 | ♀ | Femur, shaft..... | Recent fracture..... | Periosteal sarcoma | Periosteal sarcoma |
| 11 | 1916 | 19 | ♂ | Femur, lower end | Blow from block of ice; swelling 4 days later | Periosteal sarcoma | Periosteal sarcoma |
| 12 | 1915 | 15 | ♂ | Femur, lower end | Bruise, 4 weeks..... | Periosteal sarcoma | Periosteal sarcoma |
| 13 | 1917 | 28 | ♀ | Femur, lower end | No..... | Periosteal sarcoma | Periosteal sarcoma |
| 14 | January, 1920 | 22 | ♂ | Femur, midshaft | Recent fracture..... | Sarcoma..... | Sarcoma..... |
| 15 | 1921 | 5 | ♀ | Femur, lower end | None..... | Osteogenic sarcoma | Sarcoma..... |
| 16 | 1919 | 9½ | ♀ | Femur, upper end | Kick, 2 weeks..... | Periosteal sarcoma, endothelioma | Periosteal sarcoma |
| 17 | June, 1919 | 6 | ♂ | Femur, upper end | Yes..... | Periosteal; metastasis in parietal region | Periosteal sarcoma |
| 18 | January, 1917 | 26 | ♂ | Femur, upper and middle portion | Recent fracture..... | Periosteal sarcoma | Periosteal sarcoma |
| 19 | July, 1921 | 44 | ♀ | Femur, upper end | Fall, few weeks..... | Myeloma..... | Sarcoma; pathologic fracture |
| 20 | 1918 | 35 | ♂ | Femur, lower end | Fall, few weeks..... | Sarcoma..... | Periosteal sarcoma |
| 21 | 1906 | 12 | ♀ | Femur, lower third | None..... | Sarcoma; treated for rheumatism and tuberculosis 1 year | Inconclusive at that date, 1906 |
| 22 | 1912 | 27 | ♂ | Femur, upper half | Local injury 1½ years before; pain soon after; tumor 1 year later | Periosteal sarcoma; whole upper half | Periosteal sarcoma |

Radium and Toxins or Amputation and Toxins

Microscopic Diagnosis

Fibrosarcoma

Duration

2 weeks only; circumference 1½ inches (3.1 cm.) larger than normal size

Treatment

Toxins 10 days; no effect; hip joint amputation (Coley); no toxins after

Immediate Result

Recovery

Final Result

Lung, metastases months later;

Inconclusive; infiltration of vessels with large round cells suggesting sarcoma but which might well be tuberculosis (Ewing)

4 months pain; swelling soon after

Exploratory operation; tumor gross appearance typical sarcoma; toxins only treatment given (3 to 4 months)

Recovery

Well 10 years later

Alveolar sarcoma; chiefly round cells; very malignant

3 months.....

Amputation at hip (Coley) April 5, 1937; no toxins after amputation

Recovery

Lung metastases months later;

Round cell sarcoma

Few months.....

Toxins (Coley) 2 months; given by Dr. Williamson

Tumor disappeared; limb saved

Well 15 years later

Spindle cell osteogenic sarcoma

2 months.....

Local removal, June, 1939 (Coley); recurred in 4 months; hip joint amputation; toxins (Coley) after both operations

Tumor arose from periosteum; bone itself not involved at first operation; remained well 2½ years, then developed metastases

Died 3½ years onset

Mixed round and spindle cell sarcoma (Ewing)

Few months.....

Amputation; toxins 2 to 3 weeks

Recovery

Not traced

Spindle cell sarcoma

3 months.....

Amputation after 2 months; toxins and radium given for 6 months after operation

Recovery; no recurrence..

Well 6 years later

Mixed, round and giant cells

6 weeks.....

Exploratory operation; toxins 2 weeks; amputation; 30 injections of toxins; recurrence, hip joint amputation

Metastases in lung 11 months later

Died

Osteosarcoma

2 months.....

Amputation followed by 17 injections of toxins

Recovery

Not traced

Cavernous and myeloid giant cell sarcoma; sclerosing central osteogenic sarcoma of Virchow (Ewing)

.....

Amputation

Lung metastases 6 months later

Died

Chondrosarcoma .

1 month.....

Nine roentgen-ray treatments; 12 doses of toxins (Coley); amputation

Recovery; later lung metastases

Died, June 30, 1916

Osteosarcoma

1 year.....

Eleven doses of toxins; no effect; amputation, Oct. 8, 1916, followed by toxins (17 doses)

.....

Not traced

Osteogenic sarcoma

1½ years.....

Amputation after failure of radium and toxins; toxins 4 months after operation

Recovery; no recurrence..

Well 9 years later

Malignant, telangiectatic, osteogenic sarcoma

4 months.....

Toxins and radium.....

.....

Well 7 years later

Endothelioma or endothelial myeloma (Ewing)

14 months.....

Toxins and radium.....

.....

Metastases of lung, ilium and sarcoma

Died in less than year

Well 17 years later

10 months.....

Toxins and radium from October, 1917, to July, 1918

Disappearance of metastases in parietal and occipital regions; diminution in exophthalmos; no recurrence of tumor in femur; general health excellent

Well 8 years later

Perithelial sarcoma or plasma cytoma (Mandlebaum); endothelioma; malignant (Ewing)

1½ years; paralysis

Toxins; 1 radium pack, toxins continued by home physician

Entire disappearance of tumor; pathologic fracture reunited; limb saved

Metastases 2 years later; died

Spindle cell, osteogenic sarcoma

6 months.....

Toxins for 5 months and radium (about 60,000 millicurie hours) cast (elsewhere); plaster exploratory operation; April 7, 1930, amputation; toxins kept up for 4 months

Refused further treatment

Died 1 year later

Malignant chondrosarcoma (Ewing)

Pain 1½ years; tumor only 3 months; very rapidly growing

Regarded inoperable by several surgeons; hip joint amputation March 20, 1933 (Coley); saline infusion after operation; toxins (Coley) given 4 months after operation

Recovery

In good health July 1934, 2½ years later 3 weeks later (full history in text)

Well 3 years later

TABLE 7.—Group I: Patients Treated by Toxins or

| Case | Date | Age | Sex | Locality | Trauma | Clinical Diagnosis | Roentgen-Ray Diagnosis |
|------|------------------------------|-------|-----|--------------------------------------|---|--|------------------------|
| 12 | May, 1904 | 35 | ♀ | Femur, lower end | Severe blow in 1900; tumor 2 years later | Periosteal sarcoma | Periosteal sarcoma |
| 14 | 1901 | 16 | ♀ | Femur, lower end | None..... | Sarcoma..... | Probably sarcoma... |
| 15 | November, 1906 | 19 | ♂ | Femur, shaft..... | None..... | Periostitis or osteomyelitis; fusiform enlargement of nearly entire shaft (sarcoma, Coley) | Osteomyelitis..... |
| 16 | May, 1906 | 23 | ♂ | Femur, lower third | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 17 | February, 1902 | 19 | ♂ | Femur, shaft, lower two thirds | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 18 | March, 1907 | 9 | ♀ | Femur, lower end | Fall from bicycle; 2 to 3 weeks after | Periosteal sarcoma | Periosteal sarcoma |
| 19 | August, 1905 | 13 | ♀ | Femur, lower end | Fall; swelling 2 weeks later | Periosteal sarcoma | Periosteal sarcoma |
| 20 | October, 1908 Sear's case | 10 | ♀ | Femur, lower end | Fall on hard floor; pain and swelling soon after | Periosteal sarcoma | Periosteal sarcoma |
| 21 | 1905 and 1904 Rehn's case | Adult | ♂ | Femur, lower end | ?..... | Sarcoma..... | ?..... |
| 22 | December, 1907 | 25 | ♂ | Femur, shaft, middle and upper third | ?..... | Periosteal sarcoma | Sarcoma..... |
| 23 | September, 1906 | 15 | ♂ | Femur, lower end | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 24 | July, 1907 | 11 | ♀ | Femur, lower end | Fell down stairs, injuring knee; tumor 3 months later | Periosteal sarcoma | None..... |
| 25 | October, 1905 | 6 | ♂ | Femur, lower end | None..... | Periosteal sarcoma | None..... |
| 26 | January, 1909 | 22 | ♂ | Femur, shaft..... | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 27 | 1902 | 15 | ♀ | Femur, lower end | Sprain 2 weeks before | Periosteal sarcoma | Periosteal sarcoma |
| 28 | 1905 | 15 | ♀ | Femur, lower end | Recent fracture..... | Periosteal sarcoma | Sarcoma..... |
| 29 | 1902 | 25 | ♂ | Femur, lower end | None..... | Periosteal sarcoma | Periosteal sarcoma |

Radium and Toxins or Amputation and Toxins--Continued

| Microscopic Diagnosis | Duration | Treatment | Immediate Result | Final Result |
|---|---|---|---|--|
| Biopsy report: myositis ossificans (Ewing) or chronic formative osteitis. giant cell sarcoma | Injury, 1908; tumor, 1908; no pain | In view of gross and microscopic examination of specimen removed at biopsy showing no evidence of malignancy, no treatment was given in 1909 | | |
| Giant cell sarcoma | Pain, 3 months; tumor, 2 months | Toxins 1 month; decrease in size 1 inch (2.5 cm.); later increase; amputation (Coley) (Hospital for Ruptured and Crippled) May 18, 1906 | Toxins after amputation, 32 doses; rapid gain in weight | Remained well for 3 years, then developed metastases in pelvic bones and lung; died in 3½ years |
| Round cell sarcoma (biopsy) | Pain, 1 year; tumor, 2 months; loss of weight; temperature, 102 F. | Toxins (Coley) begun January, 1907; circumference of tumor decreased from 11¼ to 9½ inches (29.7 to 25 cm.); 57 injections of toxins in 1907 | Did very well for a year, then developed metastases of brain with exophthalmos, double, no recurrence of femur tumor | Died 1½ years after treatment |
| Lower end of femur hard, ivory-like formation; narrow cavities obliterated; cells few and elongated; spindle shaped tissue; does not appear very active (Ewing) | Pain and disability 10 years before; tumor soon appeared; local removal 8 years before; second operation, January, 1916 (Deaver); pathologic diagnosis: osteoma; recurred promptly 3½ months..... | Toxins (Coley) 8 doses; no improvement; amputation below trochanter (Coley), July 8, 1916; toxins kept up 2 to 3 months after operation | Recovery | Remained well for 3 years, then developed lung metastases; died |
| Round cell sarcoma (Dr. E. K. Dunham, Carnegie Laboratory) | | Hip joint amputation advised and refused; 4 roentgen-ray treatments, February to December, 1902; metastases in pelvic region in 1903; 3 to 4 inches (7.6 to 10.1 cm.) removed; pronounced round cell sarcoma; also extensive metastatic tumor in ilium, January, 1903, toxins (Coley) given at this time; 86 injections in 6 months, 170 roentgen rays to ilium | Large tumor in ilium broke down; incision and drainage; complete disappearance; tumor of thigh showed epithelioma and large round cell sarcoma; tumor in medullary cavity of bone epithelioma | Well May, 1912, 10 years later; then developed tumor in old roentgen-ray burn; excision; pronounced epithelioma; extensive tumor developed in soft part of burn; amputation at thigh, January, 1913; died; metastasis of lung 2 to 3 weeks later |
| Mixed spindle and round cell sarcoma | Tumor observed only 1 week (father a physician); one side 2 inches (5 cm.) larger than other | Toxins 2 weeks, then amputation below trochanter (Coley); toxins resumed | Recovery | Developed lung metastases 13 months later; died |
| Osteosarcoma | 6 weeks..... | Amputation below trochanter August 31, 1906; toxins for 4 months after | Recovery | Well 4½ years, then developed metastases in pelvis and lungs; died Dec. 3, 1910 |
| Osteogenic sarcoma (Ewing) | 6 months pain; tumor soon after | Amputation below trochanter (Dr. A. I. Bevan); toxins (Coley) for 9 months after amputation | Recovery | In good health December, 1924, 18 years |
| Osteosarcoma | Few months..... | Hip joint amputation (Dr. J. A. Wyeth) 1908; toxins short time under Dr. Coley's direction; well 3½ years | Recurrence in stump and iliac fossa; toxins resumed; tumor broke down; drained | Well several years later |
| Small round cell sarcoma | Few months..... | Partial local incision before coming to Memorial Hospital; regarded as inoperable; toxins for 3 months | Considerable improvement; amputation shortly after by D. J. Bolling Lee | Well 2 years later |
| Round cell sarcoma (biopsy) | 6 months pain..... | Amputation below trochanter (Dr. John Erdman) September, 1906; toxins (Coley) 3 to 4 months | Recovery | Well, July, 1926, 16 years later |
| Round cell sarcoma | 2 months..... | Hip joint amputation (Coley), July, 1897; no toxins after operation | Recovery | Not traced beyond 6 months |
| Small round cell sarcoma | 6 months..... | Amputation hip joint (Coley); no toxins | Recovery | Lung metastases 6 months later; died |
| Round cell sarcoma (Presbyterian Hospital laboratory); endothelioma (Ewing) | Few weeks; local removal (Dr. Hortenwell) August, 1909; recurred; treated at Memorial Hospital with toxins, December, 1909; improved, then increased; amputation (Dr. J. A. Blake) | Referred back to Coley for toxins after amputation; toxins given in two periods for 4 months | Recovery | Well, December, 1924, 15 years later |
| Periosteal spindle cell sarcoma | 3 months..... | Amputation below trochanter; refused toxin treatment as prophylactic | Local recurrence 3 years later | Died 6 months later |
| Osteogenic, spindle and round cell sarcoma | 3 months..... | Hip joint amputation (Coley); no prophylactic treatment | Metastases in lungs 4 months later | Died |
| Round cell sarcoma | 6 months..... | Amputation (Dowd) | Metastases in lung 14 years later | Died |

TABLE 7.—Group 1: Patients Treated by Toxins or

| Case | Date | Age | Sex | Locality | Trauma | Clinical Diagnosis | Roentgen-Ray Diagnosis |
|------|---------------------------------|-----|-----|-------------------------------|---|---|---|
| 1 | 1911 | 37 | ♂ | Femur, lower end | Severe blow; soon... | Periosteal sarcoma | Periosteal sarcoma |
| 2 | 1912 | 14 | ♂ | Femur, shaft..... | Fracture at age of 4 years; fracture at 11 years; periostitis at 21 years | Periosteal sarcoma | Sarcoma..... |
| 3 | June, 1914 | 64 | ♀ | Femur, lower end | Fall 2 months before | Sarcoma..... | Sarcoma..... |
| 4 | August, 1919 | 13 | ♀ | Femur, shaft..... | Fall, followed by swelling 1 month later | Sarcoma..... | Periosteal sarcoma |
| 5 | December, 1919 | 6 | ♂ | Femur, lower end | | Periosteal sarcoma | Periosteal sarcoma |
| 6 | January, 1920 Packard's case | 5 | ♂ | Femur, upper end | Fall; tumor soon after | Sarcoma (negative Wassermann and Pirquet reactions) | Osteosarcoma..... |
| 7 | March, 1925 | 29 | ♂ | Femur, shaft, upper third | Severe squeeze in subway door; swelling soon after | Osteoma..... | Sarcoma ?..... |
| 8 | April, 1925 | 21 | ♀ | Femur, midshaft | Automobile accident; local injury few weeks | Periosteal osteosarcoma | Periosteal sarcoma with marked production of new bone |
| 9 | January, 1925 | 50 | ♂ | Femur, midshaft | None..... | Osteomyelitis..... | Osteomyelitis..... |
| 10 | 1925 | 25 | ♂ | Femur, midshaft | ?..... | Periosteal sarcoma | Periosteal sarcoma |
| 11 | 1925 | 25 | ♂ | Femur..... | Severe strain..... | Periosteal sarcoma | |
| 12 | 1925 | 23 | ♂ | Femur, middle and upper third | Injured thigh..... | Periosteal sarcoma | Sarcoma..... |
| 13 | 1925 | 16 | ♀ | Tibia..... | Fall 3 years before | Sarcoma..... | |
| 14 | 1915 | 16 | ♀ | Tibia..... | Fall through ice..... | Periosteal sarcoma | |
| 15 | February, 1929 | 17 | ♂ | Tibia, midshaft... | None..... | Periosteal sarcoma | None..... |
| 16 | April, 1929 | 19 | ♂ | Tibia, lower end | Sprain 4 years before | Sarcoma..... | Inconclusive, probably sarcoma |
| 17 | June, 1929 | 20 | ♀ | Tibia, upper end | None..... | Osteitis..... | Doubtful..... |

Radium and Toxins or Amputation and Toxins—Continued

| Microscopic Diagnosis | Duration | Treatment | Immediate Result | Final Result |
|--|---|--|---|--|
| Myxosarcoma | 1 year..... | Toxins 4 weeks; amputation | Well few months later.... | Not traced |
| Large spindle and giant cell sarcoma (Ewing); spindle cell osteogenic sarcoma (Wood) | Enlargement noticed 2 months before operation | Local removal; curettage; roentgen-ray treatments; temporary improvement; toxins and radium (2,000 millicurie hours at 2 cm. distance); no improvement; amputation followed by toxins for a number of months | Recovery | Well 10 years later |
| | Pain 2 months..... | High voltage roentgen rays (4 treatments); toxins | No improvement | Metastases 5 months later; in this case the disease was very far advanced when treatment was begun |
| No biopsy | Swelling 5 months | Radium (31,416 millicurie hours); toxins, 18 injections; amputation advised but refused | Not improved | Not traced |
| No biopsy | | Toxins; radium (101,693 millicurie hours); roentgen rays, 12 treatments in 1 month | Rapid generalization of disease; metastases in head and lungs | Died in July, 1920 |
| No biopsy; too far advanced for exploratory operation | 3 months severe pain; extensive destruction upper third femur; patient emaciated and bedridden, quite inoperable; bed sores; dilation superficial 4 months..... | Toxins (Coley) begun by Dr. Packard, Denver, Jan. 6, 1920; kept up until June 30, 1920; 93 doses | Immediate and rapid improvement March 1; no pain; patient in wheel chair; bed sores healed; dilated veins disappeared; June 15, walked with crutches; October 1, discharged in normal health | October 1, plaster spica; January, 1921, able to work; in good health 5 years later |
| 1. Mixed cell sarcoma (Jeffries); 2. Osteogenic sarcoma, polygonal cell, malignant (Ewing) | No biopsy | Osteotomy at Jewish Hospital; toxin treatment at Hospital for Ruptured and Crippled | Entire disappearance of tumor; patient in excellent condition 3 months later | Well, July, 1926 |
| No biopsy | 3 to 4 weeks..... | Roentgen rays; 2 weeks later, toxins and radium | Decreased $\frac{3}{4}$ inch (1.8 cm.) in size; no further improvement; amputation advised and refused | Not traced |
| Osteitis, biopsy 1; osteitis, biopsy 2; sarcoma, biopsy 3; sarcoma, endothelial myeloma type (Ewing) | 5 months..... | (1) Exploratory operation and curettage August, 1924; (2) exploratory operation and removal of bone January, 1925; (3) exploratory operation July, 1925; (4) amputation July 30, 1925 (B. L. Coley); had few doses toxins before amputation, while getting consent to amputate; toxins after amputation | Recovery | Well at present time, July, 1926 |
| Biopsy: endothelioma (Ewing) | Few weeks..... | Ruptured and Crippled; not much improvement; amputation advised, refused; left hospital | Was treated elsewhere; character of treatment not known | Died about 3 months later |
| Periosteal sarcoma | 3 months..... | Amputation of hip joint (Drs. W. T. Bull and W. B. Coley) | Recovery | Died in 8 months; metastases of lung |
| Round cell sarcoma | 8 months..... | Curettage; toxins at periods (2 months and 5 weeks) | Recovery | Well 16 years later |
| Round and spindle cell sarcoma, giant cell | 2 years..... | Exploratory operation; amputation by Dr. Wm. T. Buel | Recovery | Died 6 years later, lung metastases |
| Mixed cell sarcoma | 3 months..... | Two operations by Dr. W. Lindes; roentgen rays and toxins before second operation | Recovery | Well 11 years later |
| (Prof. John Cawren, Toronto University) spindle cell sarcoma | First noticed tumor of tibia, July, 1897, operation (Dr. Stewart of Toronto) November, 1898; local removal, slow healing, recurrence in 6 weeks | Amputation advised by several surgeons; admitted to Memorial Hospital, February, 1899; later while in hospital developed typical attack of erysipelas over affected leg | Ulcerated area healed; evidence of tumor disappeared; regained health | In good condition, limb saved, well, July, 1926, 27 years later |
| Biopsy: round cell sarcoma | July, 1905, pain; December, 1905, unable to work because of limp | Exploratory operation; bone marrow absent for 6 inches (15.2 cm.) above malleolus, re-swelling of lower half of tibia; toxins (Coley) April to July, 1906 | Tumor decreased 1 inch (2.5 cm.) in size | Well when last seen more than 1 year later; unable to trace further |
| Biopsy: chondrosarcoma | Pain 6 months; tumor 1 year | January, 1907, admitted to Hospital for Ruptured and Crippled; first operation, Newburg Hospital, August, 1906, called cyst; second operation, Hospital for Ruptured and Crippled, tumor size of egg, reddish pulp like material seen in giant cell sarcoma; toxins, January to September, 1906; roentgen rays three times a week for 2 months | Rapid recurrence apparently controlled by treatment; later increase in size; amputation advised in June, but patient would not give his consent until October; performed by Dr. R. Whitman; toxins after amputation | Metastases 1 year later; died |

TABLE 7.—Group I: Patients Treated by Toxins or

| Case | Date | Age | Sex | Locality | Trauma | Clinical Diagnosis | Roentgen-Ray Diagnosis |
|------|--------------------|-----|-----|---------------------------------|--|---|---|
| 57 | Oct. 1917, 1913 | 30 | ♂ | Tibia, upper end | Wrenched knee playing golf 1 year before; no tumor until 10 months later | Sarcoma, malignant | Central sarcoma..... |
| 58 | Jan., 1913 | 27 | ♀ | Tibia, shaft..... | Fall 2 months before | Periosteal sarcoma | Periosteal sarcoma |
| 59 | March, 1913 | 12 | ♀ | Tibia, shaft..... | Local injury August, 1911; swelling 3 months later | Sarcoma ? syphilis ? | Inconclusive..... |
| 60 | December, 1911 | 17 | ♂ | Tibia, upper end | No definite trauma | Central sarcoma with periosteal involvement | Central sarcoma..... |
| 61 | January, 1913 | 35 | ♂ | Tibia, upper end | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 62 | August, 1915 | 21 | ♀ | Tibia, upper end | None..... | Central sarcoma..... | Central sarcoma..... |
| 63 | October, 1916 | 8 | ♀ | Tibia, shaft, middle two thirds | None..... | Osteitis or periostitis, periosteal sarcoma ? | Irregularity and thickening of periosteum |
| 64 | April, 1917 | 20 | ♂ | Tibia, middle and lower third | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 65 | April, 1919 | 16 | ♂ | Tibia, upper end | None..... | Periosteal sarcoma | Periosteal sarcoma |
| | December, 1912 | 19 | ♂ | Tibia, upper end | Fell from ladder, injuring upper part of tibia. tumor in 1 week | Periosteal sarcoma | Periosteal sarcoma |
| 66 | Jan., 1912 | 22 | ♀ | Tibia, lower end | None..... | Central sarcoma..... | Central sarcoma..... |
| 67 | July, 1912 | 20 | ♂ | Tibia, middle and upper third | Fracture 4 years before | Sarcoma, resembles endothelioma (Coley) type | Extensive destruction of bone involving both central and periosteal portions (Dr. D. Quirk) |
| 68 | Oct. 1911, 1911 | 15 | ♀ | Tibia, upper end | Local injury; struck by baseball 1 week | Periosteal sarcoma | Periosteal sarcoma |

Radium and Toxins or Amputation and Toxins—Continued

| Microscopic Diagnosis | Duration | Treatment | Immediate Result | Final Result |
|---|---|--|--|---|
| Spindle cell central osteogenic sarcoma; few atypical giant cells; tumor more malignant than ordinary central sarcoma of epulis type (Ewing) | 2 months..... | Exploratory operation. Oct. 24, 1913; toxins begun October 27; patient extremely nervous and in great pain; only few doses toxins given before pain was relieved; slight decrease in size | Nov. 17, 1913, pain returned; slight increase in size; amputation Nov. 22, 1913 (Coley); patient refused further toxin treatment | June, 1915, extensive metastases in ribs; died few months later |
| Round cell sarcoma | 14 months..... | Large tumor involving whole central part of tibia; toxins 3 to 4 weeks, then amputation at mid thigh (Coley); toxins 1 month after operation | October, 1910, recurrence in stump | Metastases in lung following year; died |
| Small round cell sarcoma | 1 year..... | First operation. December, 1912 (Dr. G. D. Stewart); condition believed to be syphilitic; no microscopic examination; biopsy, Jan. 3, 1913; Feb. 3, 1913, amputation (Dr. Stewart); toxins after amputation (Coley) | Recovery; toxins continued by family physician for few weeks | Died; metastases 1 year later |
| Very malignant sarcoma; mixed large polyhedral giant cells with much hyaline substance (Ewing) | 2 months..... | First operation 1 week after swelling noticed, by Dr. Mc Lane, Scranton, Pa.; cavity upper end of tibia containing soft red mottled tissue, had broken through bony structure; local recurrence 1 month; admitted Hospital for Ruptured and Crippled, Dec. 15, 1921 | Toxins and radium 3 weeks; no improvement; amputation (Dr. B. L. Coley) Jan. 15, 1922; toxins a short time after operation | Metastases in lungs; died, October, 1921 |
| Chondrosarcoma; many mononuclear giant cells (Ewing) | 2 months..... | Six doses toxins (Coley) given before operation; no improvement; amputation (Dr. Brownlee, Danbury, Conn.) Feb. 8, 1915; toxins given few weeks after amputation | Recovery | Lung metastases 6 months later; died |
| Round cell osteosarcoma; considerable malignancy (Ewing); final report: spindle cell sarcoma | 5 months..... | Biopsy, April 1, negative; biopsy, June 15, negative; biopsy, Aug. 8, 1915, central tumor not involving joint; toxins 3 months, no improvement; amputation (Coley) March, 1916 | Recovery; metastases in pelvic bones 6 months later; grew to enormous size | Died 1 year after amputation |
| Small round cell sarcoma (Ewing) | 4 months..... | Toxins begun October 30; radium pack (3,000 millicurie hours at 6 cm. distance) November 14; two other radium treatments November and December | Very rapid disappearance of tumor; February, 1917, leg practically normal; March, 1917, recurrence | Died, lung metastases, July, 1917 |
| 1, small spindle cell osteogenic periosteal sarcoma (Ewing); tumor of quite malignant structure; 2, metastatic tumor examined September, 1917; actively growing sarcoma (Ewing) | 3 weeks..... | Toxins begun April 7, 1917; radium May 1-8, 1921; June 19, a total of 46,720 millicurie hours at 6 cm. distance; decrease in size 1 inch (2.5 cm.) in first month; toxins kept up until August, then discontinued until September, 1923 | Tumor entirely disappeared by June, 1917; September 23, extensive metastases in femoral, inguinal and iliac glands; toxins resumed and radium applied to groin and iliac fossa in October, November and December, total of 47,970 millicurie hours at 10 cm. distance; toxins kept up 24 hours | Patient in good health December, 1924, 9 years later; limb saved |
| Large polyhedral cell sarcoma resembling perithelioma; no bone production (Ewing) | Few months..... | Toxins, April to September, 1919; marked improvement at first, then slight increase in size; radium treatment Sept. 19, 1919; toxins and radium kept up until June, 1920; tumor not controlled; amputation (Coley) Aug. 18, 1920; toxins after amputation | Recovery | March 1, developed metastases in skull and mediastinum and probably lungs; died 1 month later |
| Periosteal chondrosarcoma (Ewing) | 3 weeks..... | Amputation, Dec. 22, 1922 (Dr. Kleinberg, Hospital for Ruptured and Crippled); toxins (Coley) after operation, kept up for 2 to 3 months; roentgen-ray examination Nov. 13, 1923, for first time, showed metastases in left lung; toxins resumed; September, roentgen-ray treatment to chest | Metastatic nodules on lung controlled by toxins and radium until April, 1924; condition then grew worse | Died in beginning of 1925 |
| Osteosarcoma; not the so-called giant cell sarcoma giant cell, Ewing (Mandlebaum) | Slight increase in size 6 years before; recent increase in size | Operation, March, 1922 (Dr. H. Liffenthal), curetted tumor and implanted fat; toxins given soon after operation and continued later by Drs. Coley and S. Stedman of San Francisco | Recovery; no recurrence | Well, August, 1926, 4 years later, limb normal |
| No biopsy | Pathologic fractures 2 weeks before; pain few days before | Toxins and radium treatment (Memorial Hospital, Coley) | Complete recovery | Patient well, July, 1926, 7 years later |
| Sarcoma, osteogenic | | Toxins and radium 2 months; tumor not controlled; amputation (Dr. B. L. Coley) Oct. 21, 1921; toxins after amputation | Recovery | In good health, July, 1926, 4 years 10 months later |

TABLE 7.—Group 1: Patients Treated by Toxins or

| Case | Date | Age | Sex | Locality | Trauma | Clinical Diagnosis | Roentgen-Ray Diagnosis |
|------|---------------|-----|-----|--------------------|---|---|---|
| 1 | Feb. 27, 1914 | 14 | ♂ | Fibula, upper end | | Periosteal sarcoma | Periosteal sarcoma |
| 2 | March, 1919 | 9 | ♂ | Fibula, lower end | January, 1920, blow to outer side leg; pain few days later; swelling soon after | Osteomyelitis (Hospital for Ruptured and Crippled); sarcoma, very extensive (Coley) | Periosteal sarcoma; metastases |
| 3 | April, 1918 | 21 | ♂ | Fibula, upper end | ?..... | Periosteal sarcoma | Periosteal sarcoma |
| 4 | August, 1920 | 12 | ♂ | Fibula, upper end | None..... | Osteomyelitis following operation for suppurating appendicitis | Doubtful at first; periosteal sarcoma; Aug. 8, 1920, roentgen rays showed no recurrence |
| 5 | 1921 | 14 | ♂ | Fibula, upper end | None..... | Periosteal sarcoma | Periosteal sarcoma; suggested possible endothelioma |
| 6 | 1921 | 16 | ♂ | Tibia, upper end | | Periosteal sarcoma | Periosteal sarcoma |
| 7 | 1918 | 20 | ♀ | Fibula..... | ?..... | Periosteal sarcoma | None..... |
| 8 | June, 1917 | 7 | ♀ | Tibia, midshaft | No..... | Periosteal sarcoma | Periosteal sarcoma |
| 9 | May, 1915 | 6 | ♀ | Tibia, upper end | Six months before injured in automobile accident; tumor 4 months later | Periosteal sarcoma | Periosteal sarcoma |
| 10 | March, 1915 | 13 | ♀ | Tibia, upper end | Three months..... | Periosteal sarcoma; first diagnosis: syphilitic periostitis | Periosteal sarcoma; first roentgenogram: syphilis |
| 11 | 1915 | 23 | ♀ | Humerus, upper end | Few months..... | Periosteal sarcoma | None..... |
| 12 | 1916 | 15 | ♀ | Humerus, upper end | Old injury 10 years before | Periosteal sarcoma | Periosteal sarcoma; really inoperable as it was impossible to get around tumor by operation |
| 13 | March, 1917 | 19 | ♂ | Humerus, upper end | Fell on ice; fracture 5 weeks before | Central sarcoma, malignant | Central sarcoma..... |
| 14 | Oct. 2, 1916 | 11 | ♀ | Humerus, upper end | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 15 | Feb. 27, 1914 | 14 | ♀ | Humerus, upper end | None..... | Periosteal sarcoma | Periosteal sarcoma |

Radium and Toxins or Amputation and Toxins—Continued

| Microscopic Diagnosis | Duration | Treatment | Immediate Result | Final Result |
|--|--|---|---|--|
| Osteogenic sarcoma (Ewing) | 6 weeks pain..... | Toxins and radium (Memorial Hospital, Coley) Oct. 28, 1924 for 3 weeks, no improvement; amputation advised, refused; resection (Dr. Fred Albee) December, 1924; referred back to Dr. Coley for toxins after operation | Operation showed extensive osteogenic sarcoma with separate nodules in muscles of calf; recovery in 1925; amputation (Coley) | Well at present, July, 1926 |
| Round cell sarcoma (Jeffries and Ewing); revised diagnosis: endothelioma (Ewing); tumor in groin; round cell sarcoma | 6 weeks..... | Biopsy March, 1920; clinical and microscopic diagnosis: osteomyelitis, round cell sarcoma, very rapid growth, enlarged glands in groin; amputation (Dr. R. Whitman) June 1, 1926; toxins (Coley) June to August | Growth in groin excised; microscopic diagnosis: sarcoma; October 27, extensive metastatic tumor in iliac fossa, 1 dose radium (10,108 milliecurie hours); lung metastases October, 1920 | No further treatment; complete recovery; well July, 1926, 6 years 4 months later |
| Biopsy: malignant osteogenic sarcoma, giant cell (Ewing) | | Toxins and radium 2 months; no improvement; amputation (Coley) followed by toxins | Recovery | Metastases in lung 8 months later; died |
| Chondrosarcoma, cellular, malignant (Ewing) | 5 months..... | First operation, scraping bone, January, 1920; recurrence 2 months; resection 6 inches (15.2 cm.) shaft, August, 1920; local recurrence; third operation, whole fibula removed except little piece near knee joint; toxins and radium August, 1920; radium pack (44,029 milliecurie hours) and bare tubes | Roentgen-ray examination, December, 1920, showed calcareous areas site of fibula; possible recurrence April, 1921; undoubted recurrence; amputation (Coley) April 6, 1920; toxins after operation | Metastases in lung; died, September, 1921 |
| Osteogenic sarcoma (Ewing) | Small size swelling in few weeks | Toxins and radium at Memorial Hospital, 3 months (Coley) | Marked improvement; while still improving locally, developed metastases in lungs 3 to 4 months later | Died 6 months later; metastases in lung and local recurrence |
| Osteogenic sarcoma (Ewing) | Few weeks..... | Toxins and radium 3 months at Hospital for Ruptured and Crippled; marked improvement soon noted; tumor disappeared in 4 months | Developed local radium burn | Two years later developed activity in tuberculous process in lung; no recurrence of sarcoma 5 years later; limb saved; lung condition progressed; died, November, 1925 |
| Spindle cell sarcoma | 6 months..... | Toxins few weeks; later amputation | | Died; metastases in lung in less than 1 year |
| 1, periosteal sarcoma (pathologist Toronto General Hospital); 2, diffuse endothelioma (Ewing) | 6 months..... | Roentgen-ray radiation before coming to Memorial Hospital, then toxins, amputation and toxins | Prompt recovery | Well 8 years later |
| Osteochondrosarcoma | 4 months..... | Biopsy, April 5, 1925, by Dr. Cunningham Wilson; four roentgen-ray treatments (deep therapy) to groin | Rapid increase in size in spite of roentgen rays; amputation, May 9, by Dr. W. B. Coley, followed by prophylactic toxins | Died, metastases of lung, September, 1925 |
| Osteogenic sarcoma (Ewing) | 4 weeks..... | Treated 4 weeks with toxins and radium (Coley); no effect; amputation advised and refused; roentgen ray and radium given elsewhere 3 months | Readmitted to Hospital for Ruptured and Crippled, June 1, 1925; amputation by Dr. B. L. Coley, followed by toxins | Well, August, 1926 |
| Osteosarcoma, large, round cell (F. B. Mallory) | Few months..... | Interseapular thoracic amputation advised but refused; exploratory operation (Dr. Blake) glenoid portion of scapula involved; prolonged toxin treatment under Dr. Coley's direction | Complete recovery; restoration of function; limb saved | In good health for 24 years, then developed metastases in spine; died |
| Round cell sarcoma | Pain 6 months; swelling 5½ months | Very extensive tumor involving two-thirds of humerus; toxins for 2 weeks; amputation, interseapular thoracic (Coley), July, 1907; toxins for 2 or 3 months | Axillary and subclavian vein filled with tumor; thrombus showing amputation did not get beyond disease and it was really an inoperable case | April, 1907, developed lung metastases; died, May 10, 1908 |
| Design giant cell sarcoma epulis type (Ewing) | 5 weeks before; believed to be redundant Colles' fascia following fracture | Immediate amputation without biopsy (Coley); clinical history and physical signs regarded as proof of highly malignant tumor | Toxins given twice a week and later once a week until September, 1920 | June, 1911, developed weakness and signs of lung metastases; died, Aug. 20, 1921 |
| Biopsy: round cell sarcoma | 3 months..... | Toxins, 3 weeks, no improvement; amputation advised by Coley but refused | Patient left hospital..... | Developed metastases few months later; died |
| Round cell sarcoma | 4 months swelling | Treated in early stage by one physician as a dislocation and some violence used to reduce it; then mechanical massage; when admitted to Memorial Hospital, Feb. 3, 1904, tumor was very large, almost inoperable; patient emaciated | Amputation (Coley) Feb. 5, 1907; recovery; toxins and roentgen rays given | Soon developed metastases in spine and probably in lungs; died June 26, 1904 |

TABLE 7.—Group 1: Patients Treated by Toxins or

| Case | Date | Age | Sex | Locality | Trauma | Clinical Diagnosis | Roentgen-Ray Diagnosis |
|------|------------------|------------|-----|--------------------|---|---|--|
| 1 | June, 1919 | 15 | ♂ | Humerus, midshaft | January, 1910, spinal fracture from fall; roentgen ray showed no pathologic condition at time; 3 weeks later, sarcoma | Periosteal sarcoma | Periosteal sarcoma |
| 26 | February, 1928 | 17 | ♀ | Humerus, shaft | Puncture of forearm 8 weeks before with needle; 1 week later swelling noted higher up in arm; probably no connection | Subperiosteal abscess | Doubtful..... |
| 27 | May, 1915 | 16 | ♀ | Humerus, midshaft | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 28 | May, 1912 | 15 | ♂ | Humerus, upper end | None..... | Periosteal sarcoma | Productive and destructive process, probably sarcoma (Cole) |
| 29 | May, 1914 | 20 | ♂ | Humerus, upper end | None..... | Inflammatory rheumatism at first, periosteal sarcoma, May, 1914, inoperable | Periosteal sarcoma |
| 30 | November, 1916 | 25 | ♂ | Humerus, upper end | Local injury 1½ years before | Bursitis after first; later, periosteal sarcoma | Tumor of soft parts with secondary involvement of periosteum (Holding) |
| 31 | October, 1916 | 26 | ♂ | Humerus, upper end | Severe blow with iron bar, upper arm, 14 years before | Periosteal sarcoma | Periosteal sarcoma |
| 32 | February, 1918 | 21 | ♂ | Humerus, upper end | Severe strain on shoulder; tumor in few weeks | Sarcoma..... | Sarcoma..... |
| | October, 1917 | 17 | ♀ | Humerus, upper end | August, 1917, fell, striking on shoulder; pain 1 month later | Periosteal sarcoma | Typical periosteal sarcoma |
| | November 2, 1918 | 19 | ♂ | Humerus, upper end | Struck point of shoulder against corner, June, 1918; 1 month later pain and stiffness | Periosteal sarcoma | Cyst with probable malignant change |
| 36 | February, 1917 | 14 colored | ♂ | Humerus, upper end | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 37 | Jan. 22, 1921 | 19 | ♀ | Humerus, upper end | None..... | Diagnosis, May 23, 1921, bursitis; June 21, periosteal sarcoma | May 24, 1921, roentgen-ray examination negative; June 21, periosteal sarcoma |

Radium and Toxins or Amputation and Toxins—Continued

| Microscopic Diagnosis | Duration | Treatment | Immediate Result | Final Result |
|---|--|---|--|---|
| Spindle cell osteogenic sarcoma (Ewing) | Severe pain 3 weeks after fracture; second roentgenogram showed well developed tumor at site of fracture | June, 1910, exploratory operation by Dr. J. M. T. Finney, who found a large sarcoma involving the periosteal and central portions; pathologic fracture; believed amputation offered little hope; referred patient to Coley for toxins; toxins begun June 9, 1910 | By November, 1910, tumor had disappeared; fracture united; December, 1910, signs of recurrence near head of humerus; amputation at shoulder joint (Coley) January, 1911; large tumor recurred in pectoral region; 6 months later, incomplete removal; prolonged toxin treatment | Patient remained well for 8 years; in 1920 he developed metastases in lungs; died in a few months |
| Osteosarcoma with spindle cells predominating (Dr. John Funke, Jefferson Hospital, Philadelphia) | 5 weeks of pain; swelling soon after | Exploratory operation, Feb. 15, 1908, by Dr. John Gibbons of Philadelphia; mass size of egg removed from lower inner surface of humerus; microscopic diagnosis: osteosarcoma; amputation advised but refused; treated with toxins under Dr. Coley's direction, combined with roentgen rays for several months | Tumor recurred in early March; disappeared under treatment | Well 16 years later; limb saved |
| Myxochondrosarcoma, biopsy, November, 1914 | 8 months..... | Roentgen rays 2 months before coming to Memorial Hospital; 2 weeks toxin treatment; Dr. Coley then advised amputation; patient left hospital; later amputation in June, 1915 | Recovery | Not traced |
| Spindle cell sarcoma (biopsy) | 2 years pain..... | Toxins for 2 to 3 weeks at Memorial Hospital; continued at home; patient refused amputation; toxins kept up 6 weeks | Improved at first; later tumor increased in size; metastases developed | Died, October, 1912 |
| Osteochondrosarcoma, malignant (Ewing) | 5 months pain; later swelling; lost 40 pounds (18.1 Kg.) weight since January | Condition believed inoperable, June 1, 1914, ligation of subclavian artery (Coley); June to August, 28 doses of toxins (Coley); decrease in circumference 1 3/4 inches (4.3 cm.) by June 28; August 11, interseapular thoracic amputation (Coley); roentgen-ray treatment and toxins after amputation | Recovery; temporary improvement; Dec. 18, 1914, metastases in liver (lungs free) | Died, May, 1915 |
| Sarcoma; tumor peculiar and different from common bone sarcoma; probable diagnosis: myxosarcoma (Ewing) | Pain soon after injury; 1 1/2 years later swelling | Amputation advised by Coley and Downes, but refused by patient; treated with toxins and radium; 40 injections of toxins; 1,800 millicurie hours radium at 3 cm. distance | No improvement | Left hospital; not traced |
| Small round cell sarcoma | 6 months swelling with little pain | Refused early amputation; treated with toxins and radium for 5 weeks (very large tumor); November, 1916, amputation by Dr. Charles Stewart of Newport, R. I.; no toxins after | Recovery | Metastases 3 months later; died |
| None | 1 month pathologic fracture; metastatic tumor in lung | February, 1918, exploratory operation by Dr. Mackid of Calgary, Canada; large amount of gelatinous tumor tissue removed; patient put on toxins (Coley) for 4 months | Wound healed; fracture reunited; tumor disappeared; toxins discontinued from July to November, then resumed for another period | Well at present, 8 years later |
| | 1 month..... | Toxins and radium at Memorial Hospital | Disease not controlled.... | Lung metastases 5 months later; died |
| Mixed cell sarcoma (Mayo Clinic laboratory) | 4 months..... | Resection upper third humerus (Mayo Clinic, Dr. H. W. Meyerding), Oct. 18, 1918; radium treatment 3 weeks then referred to Dr. Coley for toxins; toxins begun Dec. 3, 1918, and continued at home; no marked reaction | Jan. 9, 1919, roentgen ray showed large fusiform mass attached to seventh rib, bulging into chest cavity; radium pack applied (12,000 millicurie hours at 6 cm.) | Metastases developed in femur; died in about 8 months |
| Osteogenic sarcoma (Ewing) | 2 1/2 months pain and stiffness | Amputation advised and refused; Feb. 8, 1917, exploratory operation; toxins and radium for few weeks; disease not controlled; amputation (Coley) | | Metastases in lungs 6 months later; died |
| No biopsy | 5 months; loss of abduction first symptom | Baking, electricity and massage 6 weeks on diagnosis of bursitis; referred to Dr. Coley, June 24, 1924; amputation advised but refused as she was several months pregnant; toxins, radium and roentgen rays given at Memorial Hospital | Tumor apparently entirely disappeared in 2 months; recurred in October; further roentgen-ray treatment; very rapid and remarkable decrease in size; circumference over tip of clavicle and axilla diminished 5 inches (12.7 cm.) in 4 weeks; in 6 weeks arm was practically normal; toxins continued at home | Dec. 2, 1924, not increasing in size; firm metastases, summer of 1925 |

TABLE 7.—Group I: Patients Treated by Toxins or

| No. | Date | Age | Sex | Locality | Trauma | Clinical Diagnosis | Roentgen-Ray Diagnosis |
|------|-----------------|-----|-----|----------------------------------|--|--|--|
| 1.10 | July, 1921 | 17 | ♂ | Humerus, upper end | May 15, 1921, spinal fracture upper third humerus; December, 1921, swelling and pain | Periosteal sarcoma | Periosteal sarcoma |
| 1.11 | November, 1921 | 21 | ♂ | Humerus, upper end | None..... | Osteomyelitis (Hospital for Ruptured and Crippled) | Periosteal sarcoma |
| 1.12 | December, 1921 | 19 | ♂ | Radius, lower end | Repeated trauma; riveter by occupation; constant vibration of wrist | Periosteal sarcoma | Periosteal sarcoma |
| 1.13 | April, 1922 | 15 | ♀ | Radius, lower third of shaft | Severe wrench of arm 5 years before; swelling 1 year later | Periosteal sarcoma | Periosteal sarcoma |
| 1.14 | July, 1923 | 8 | ♂ | Ulna, midshaft | Fell on pile of bricks; swelling of forearm noted soon after | Periosteal sarcoma (Coley) | Syphilitic osteitis (at one hospital); "peculiar condition, diffuse rarefying process with partial occlusion of the medullary cavity; periosteum thickening" (Quick) |
| 1.15 | July, 1923 | 15 | ♂ | Ulna, upper end | Fracture 7 months; later swelling | Sarcoma..... | Sarcoma..... |
| 1.16 | September, 1924 | 22 | ♂ | Radius, lower end | None..... | Central sarcoma.... | Central sarcoma.... |
| 1.17 | 1925 | 31 | ♂ | Clavicle, middle and inner third | Severe blow from falling plank 6 to 7 years before | Periosteal sarcoma | |
| 1.18 | 1929 | 16 | ♂ | Clavicle, middle two thirds | Severe strain; swelling in 2 to 3 weeks | Periosteal sarcoma | Periosteal sarcoma |
| 1.19 | May, 1931 | 11 | ♀ | Clavicle..... | Fell, striking shoulder on hard floor February, 1924; pain and swelling 2 or 3 weeks later | Periosteal sarcoma | Periosteal sarcoma |
| 1.20 | August, 1937 | 16 | ♂ | Mastoid..... | ?..... | Sarcoma..... | Sarcoma..... |
| 1.21 | March, 1937 | 13 | ♀ | First rib, left side | None..... | Sarcoma..... | Sarcoma..... |
| 1.22 | 1938 | 15 | ♀ | Metatarsal bone | ?..... | Sarcoma..... | None..... |

Radium and Toxins or Amputation and Toxins—Continued

| Microscopic Diagnosis | Duration | Treatment | Immediate Result | Final Result |
|---|----------------------------|--|---|---|
| No biopsy | 6 months pain..... | Referred by Dr. John B. Deaver with a very large tumor of left shoulder; border line of operability; toxins directly into tumor and radium pack applied | Improvement; slight recurrence in November, 1924; further radium treatment in December, 1924 | Well, July, 1926, 2 years later |
| | 2 months..... | Exploratory operation (Coley) Nov. 19, 1917; large amount of soft reddish tumor tissue resembling myeloid sarcoma removed; thorough curetting of cavity; phenol (carbolic acid) applied; toxins and radium given in large doses | Tumor not controlled; grew rapidly | Died, Feb. 19, 1918 |
| Fibrosarcoma (Jeffries) | 3 months pain..... | Exploratory operation (Coley) Jan. 5, 1920; toxins alone 2 weeks; decrease 1½ inches (3.1 cm.) in size; toxins and radium continued until April, 1920; disease under apparent control | Patient later under Dr. J. O. Bloodgood's care; further radium treatment; metastases in axilla in August; later lung metastases | Died |
| Periosteal spindle cell sarcoma (Ewing) | 2 to 3 years..... | Treated at Massachusetts General Hospital 2 to 3 years before; roentgen rays; improvement; recurrence in 6 months; amputation advised (Dr. Monks), Jan. 27, 1913, but refused; further roentgen-ray treatment at Boston City Hospital and Boston Homeopathic Hospital; no improvement; referred to Dr. Coley April 7, 1913; toxins 3 weeks; no improvement; amputation; prolonged toxins afterward (Coley) | Recovery | Well 12 years later |
| Very cellular, infiltrating, small cell sarcoma, probably periosteal (Ewing); revised diagnosis: endothelioma (Ewing) | Few weeks..... | Exploratory operation (Hoguet and Coley); toxins and radium (Coley), 90,000 millicurie hours radium at 6 cm. distance | Almost complete disappearance of tumor; September, 1920, evidence of metastases in liver; grew worse rapidly | Died, Dec. 14, 1920 |
| Sarcoma | 7 months..... | Amputation (Dr. E. W. Lovett of Boston), July, 1908; referred to Dr. Coley for toxins after operation; toxins given 2 to 3 times a week from July to October; highest dose 5½ minims; temperature 104.5 F. | Recovery | Patient well, 1924, 16 years later |
| Round cell sarcoma of radius; ulna tumor showed giant cells not in primary tumor | 4 months..... | First operation: resection of humerus (Dr. H. Lillenthal) September, 1913; in May, 1914, developed tumor in ulna; typical roentgenogram of giant cell sarcoma; 9 doses of toxins; amputation (Dr. Lillenthal) November, 1914 | Developed lung metastases | Died, December, 1913 |
| Small round cell sarcoma | Swelling 5 months | Total excision of clavicle by Dr. Maurice H. Richardson; patient referred to Dr. Coley for prophylactic toxins; treatment kept up several months | Recovery | Well, June, 1925, 17 years later |
| Round cell sarcoma (Ewing) | Few weeks..... | Total excision clavicle (Coley) followed by prophylactic toxin treatment 3 to 4 months | Recovery | Well 15 years later |
| Endothelioma (Ewing) | 2½ months..... | Immediate total excision clavicle; buried radium, bare tubes, in wound (8 millicuries) at time of operation | Wound sloughed some at site of buried radium; toxins begun 2 weeks after operation; kept up until August, 1924 | Early in August noticed local return; massive dose of radium; toxins continued; gradual increase in size; died, Nov. 28, 1924 |
| Periosteal osteogenic sarcoma (Ewing and Mallory) | 8 months..... | Four operations by Dr. Frederic K. Lund of Boston; 2 radium treatments; referred to Dr. Coley, August, 1917; apparent recurrence at time toxins were begun; injections kept up 1 year; three roentgen-ray treatments | Recovery; no further recurrences | Patient well, July, 1926, 9 years later |
| No biopsy | 3 months pain and swelling | Toxins and radium for nearly 1 year; gradual decrease in size of tumor and replacement of destroyed area with new bone | Complete recovery | Well, January, 1925, 7½ years |
| Fibrosarcoma (New York Hospital Laboratory) | Few months..... | Amputation (Dr. W. T. Bull), 1933; recurrence in stump and popliteal space 1½ years later; treated with toxins (Coley); great improvement; 2 inch (5 cm.) amputation; later increase in swelling; second amputation (Coley); recurrence; large inoperable tumor in gluteal region; incomplete removal; toxins resumed | Remainder of tumor absorbed | Patient well, January, 1925, 32 years after first operation |

TABLE 7.—Group I: Patients Treated by Toxins or

| Case | Date | Age | Sex | Locality | Trauma | Clinical Diagnosis | Roentgen-Ray Diagnosis |
|------|------|-----|-----|-----------------|---|--------------------|------------------------|
| 100 | 1916 | 24 | ♀ | Metatarsal bone | ? | Periosteal sarcoma | None..... |
| 101 | 1912 | 12 | ♂ | Clavicle..... | Fell, striking on wood box, 1 week before | Periosteal sarcoma | Periosteal sarcoma |

TABLE 7.—Group II: Patients Treated

| Case | Date | Age | Sex | Locality | Trauma | Clinical Diagnosis | Roentgen-Ray Diagnosis |
|------|-----------------|-----|-----|--------------------------|--|---|---|
| 102 | October 7, 1924 | 17 | ♀ | Femur, lower end | Fell down stairs, injuring right knee, 10 months before | Periosteal sarcoma | Periosteal sarcoma |
| 103 | February, 1924 | 22 | ♀ | Femur, lower end | Severe blow, August, 1923; pain and swelling 2 months later | Periosteal sarcoma | Periosteal sarcoma |
| 104 | November, 1915 | 18 | ♂ | Femur, midshaft | Strain 1½ years before; swelling for months later | Periosteal sarcoma | Periosteal sarcoma |
| 105 | September, 1922 | 24 | ♂ | Femur, midshaft | Slight local trauma August 15; pain and swelling soon after | Periosteal sarcoma | Periosteal sarcoma |
| 106 | March, 1919 | 23 | ♀ | Femur, lower end | None..... | Periosteal sarcoma | Appearance suggestive of giant cell sarcoma |
| 107 | February, 1924 | 23 | ♂ | Femur, lower end | Struck thigh above knee September, 1923; pain 2 months; swelling 3 months | Periosteal sarcoma | Periosteal sarcoma |
| 108 | October, 1922 | 10 | ♂ | Femur, upper third shaft | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 109 | July, 1922 | 13 | ♀ | Femur, midshaft | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 110 | August, 1922 | 25 | ♀ | Femur, lower end | Struck above knee, November, 1921; pain followed swelling in 2 months | Periosteal sarcoma | Periosteal sarcoma |
| 111 | September, 1924 | 19 | ♀ | Femur, lower end | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 112 | March, 1923 | 45 | ♀ | Femur, lower end | Fell injuring knee 13 months before; had had pain before; swelling 1 month later | Central sarcoma, giant cell; central sarcoma, malignant (Coley) | Giant cell sarcoma... |
| 113 | January, 1922 | 45 | ♂ | Femur, upper end | ? | Central tumor, giant cell | Benign, giant cell sarcoma |
| 114 | September, 1924 | 14 | ♂ | Femur, lower end shaft | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 115 | September, 1922 | 17 | ♂ | Femur, lower end | Fell down stairs 4 years before | Periosteal sarcoma | Periosteal sarcoma |

Radium and Toxins or Amputation and Toxins—Continued

| Microscopic Diagnosis | Duration | Treatment | Immediate Result | Final Result |
|----------------------------------|-------------------|--|---|---|
| Small round cell sarcoma (Ewing) | Few months..... | Exploratory incision; amputation of leg, middle and lower third; prolonged toxins after amputation | Recovery | Well 12 years later |
| Round cell sarcoma | 1 to 2 weeks..... | Total excision clavicle (Coley) | Recovery; toxins for 2 to 3 weeks; recurrence 6 weeks later; rapid growth | Developed metastases and death occurred within 5 months from date of injury |

with Radium and the Roentgen Rays

| Microscopic Diagnosis | Duration | Treatment | Immediate Result | Final Result |
|--|---|--|--|--|
| No biopsy | 2 months; pain and swelling first symptom | High voltage roentgen rays, 3 treatments, November 3 to 11 | Nov. 3, 1923, no evidence of metastases; November 26, acute fulminating metastases; temperature 104 F. | Died Feb. 9, 1924; total duration of disease 5½ months |
| Osteogenic sarcoma | 4 months..... | High voltage roentgen rays, Memorial Hospital; bony metastases in muscle of outer part of axilla removed; proved to be osteogenic sarcoma; amputation advised but refused | Grew thin and emaciated | Died |
| Round cell sarcoma | 1 year; swelling first symptom | Treated at Bellevue Hospital (Dr. J. B. Bissell) with radium, after 10 doses of toxins; Dr. Coley advised amputation, refused | Severe deep burns; tumor apparently entirely disappeared; recurred locally 3 years later; general metastases | Further radium treatment; no effect; died, March 1919 |
| Cellular giant cell tumor (Ewing); biopsy specimen after amputation diagnosed as malignant osteogenic sarcoma (Ewing) | 1 month; pain and swelling | Radium from Sept. 9 to Nov. 3, 1922 (209,337 millicurie hours), largest dose used at Memorial Hospital | Disease not controlled; amputation, Dec. 10, 1922 (Dr. Quick) | Died few months later |
| Fibrosarcoma | 1 year pain; 6 months swelling | Radium, March, 1919, to 1920; roentgen rays, May, 1921, to September, 1921 | Disease controlled for nearly 4 years, then pathologic fracture | Amputation early in 1924; well 1½ years after amputation |
| Malignant osteogenic sarcoma | 3 months..... | Roentgen rays 2 months; swelling and pain increased; amputation (Coley), May 20, 1924; toxins for nearly year | Recovery; no recurrence | Well nearly 2½ years after amputation |
| No biopsy | 2 months; first symptom swelling; pain soon after | High voltage roentgen rays, October, 1922; no improvement; radium, bare tubes (78 millicurie hours) in tumor; total, 10,236 millicurie hours | No improvement; tumor increased in size; rapid loss of strength and flesh | Died few months later |
| No biopsy | 5 months; pain and disability; tumor 3 months | Roentgen rays July, 1922, to January, 1923 | Definite increase in density; slow increase in size; December, 1922, clinical evidence of lung metastases | Grew worse and died in February, 1925 |
| No biopsy | 7 months; pain first symptom | Sixteen electrical treatments elsewhere; 6 roentgen-ray treatments at Memorial Hospital, August to November, 1922 | No improvement; amputation advised; took high voltage roentgen rays at another hospital; no improvement; amputation early in 1924 | Well 1 year later |
| | Pain 2 months; tumor 6 weeks | Six roentgen-ray treatments at Memorial Hospital, Sept. 12 to Oct. 20, 1924; readmitted, Dec. 2, 1924 | Severe pain not controlled by roentgen rays; steady increase in size; great increase between October 24 and December 2; much emaciated | Amputation, Dec. 9, 1924 |
| Giant cell sarcoma from gross appearance of tumor and biopsy; microscopic examination after amputation: malignant large spindle cell sarcoma (Ewing) | Pain 12 months; tumor 10 months | Plaster cast for several months; later radium and roentgen rays; exploratory operation 6 months before admittance to Memorial Hospital; amputation (Dr. Martin) March 16, 1923 | Recovery | Lung metastases; died few months later |
| No biopsy at first; 8 months later recurrence; diagnosis: degenerating fibrosarcoma (Ewing) | | Treated with roentgen rays 6 months at Memorial Hospital; slow increase; curettage (Coley), August, 1923; very vascular, red, pulpy tissue closely resembling giant cell tumor | Tumor continued to grow; condition beyond hip joint amputation; great pain; loss of weight | Died of exhaustion, August, 1924 |
| No biopsy | Pain 3 years; tumor soon after | Eleven high voltage roentgen-ray treatments, February to August, 1922 | Disease not controlled; Oct. 21, 1922, amputation advised | Not traced |
| No biopsy | 2 months; severe pain first symptom | Four high voltage roentgen-ray treatments (50 minutes each), January to March, 1924 | Marked improvement; disease apparently under control, December, 1924 | Not traced |

TABLE 7.—Group II: Patients Treated with

| Case | Date | Age | Sex | Locality | Trauma | Clinical Diagnosis | Roentgen-Ray Diagnosis |
|------|----------------|------------|-----|--|--|---|--|
| 126 | May, 1915 | 10 | ♂ | Femur, midshaft | Fell on steel rail injuring mid thigh; swelling 2 months | Periosteal sarcoma | Periosteal sarcoma |
| 127 | January, 1916 | 21 | ♂ | Femur, lower third | None..... | Periosteal sarcoma | Periosteal osteosarcoma |
| 128 | February, 1922 | 18 colored | ♂ | Femur, midshaft | Kicked in mid thigh July, 1921; local pain 2 months; swelling soon after | Periosteal sarcoma | Periosteal sarcoma |
| 129 | June, 1923 | 13 | ♀ | Femur, lower end | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 130 | March, 1921 | 30 | ♂ | Femur, shaft..... | Severe blow, anterior thigh, by barrel of molasses, Nov. 13, 1920; pain few days later; lump, size of fist, soon after | ?..... (Case of Drs. Quick and Cole) | Periosteal sarcoma (Dr. Rufus Cole) |
| 131 | June, 1923 | 42 | ♂ | Femur, shaft..... | Fall from car 7 months before; lump appeared 2 months after | Periosteal sarcoma ? | Osteogenic sarcoma; suggested slowly growing and benign type |
| 132 | December, 1924 | 21 | ♀ | Femur, lower end | Six months before, struck knee on foot-press; swelling noticed immediately after | Periosteal sarcoma | Osteogenic sarcoma |
| 133 | January, 1925 | 14½ | ♀ | Femur, lower third | No history of trauma | Periosteal sarcoma | Osteogenic sarcoma, distal third of femur, Jan. 26, 1925 |
| 134 | February, 1925 | 53 | ♂ | Tibia, upper end | ?..... | Central sarcoma, clinically malignant | Central sarcoma, giant cell |
| 135 | March, 1922 | 15 | ♂ | Humerus, upper third | Fell from sled injuring arm 7 weeks before; had had pain 1 week before injury | Periosteal sarcoma | Periosteal sarcoma |
| 136 | April, 1921 | 31 | ♀ | Humerus, lower end | None..... | Periosteal sarcoma | Roentgen ray showed no bone involvement |
| 137 | August, 1920 | 44 | ♀ | Humerus, middle and upper third of shaft | None..... | Periosteal chondrosarcoma | Enchondroma, benign |
| 138 | July, 1920 | 23 | ♂ | Humerus, midshaft | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 139 | 1924 | 15 | ♂ | Humerus, upper end | None..... | Giant cell tumor ?... | Chondrosarcoma ? |
| 140 | April, 1918 | 70 | ♀ | Humerus, upper midshaft | None..... | Periosteal sarcoma | Sarcoma..... |
| 141 | October, 1923 | 40 | ♂ | Humerus, upper end | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 142 | 1922 | 14 | ♂ | Humerus, upper third | Local injury..... | Periosteal sarcoma | Periosteal sarcoma |
| 143 | 1915 | 51 | ♂ | Humerus, upper third | None..... | Sarcoma..... | Sarcoma..... |
| 144 | January, 1922 | 24 | ♀ | Humerus, upper third | None..... | Probable sarcoma... | Osteosarcoma of medullary origin |

Radium and Roentgen Rays—Continued

| Microscopic Diagnosis | Duration | Treatment | Immediate Result | Final Result |
|--|--|---|---|---|
| Round cell sarcoma | 4 months..... | Radium, Memorial Hospital..... | Reduced to one third original size; spontaneous fracture; September 1915, entered New Haven Hospital | Amputation; lung metastases; died few months later |
| No biopsy | 2 months..... | Radium, Memorial Hospital (Dr. H. H. Janeway), July to September, 1916 | Improved at first; later slight enlargement; general condition grew worse | December, 1916, lung metastases; died shortly after |
| No biopsy | 3 months..... | Roentgen rays from March 11 to Aug. 14, 1922 | Sept. 11, 1922, evidence of lung metastases noticed | Died, Sept. 20, 1922 |
| No biopsy | 2 months pain..... | Two roentgen-ray treatments, June 25 to 29, 1923 | Swelling disappeared | Not traced |
| No biopsy | 9 months..... | Roentgen-ray treatment (Dr. Cole), December, 1920, to March, 1921; radium bare tubes buried in tumor at Memorial Hospital (Dr. D. Quick) | Improvement | Well, December, 1924; clinical history favors diagnosis of myositis ossificans |
| Osteogenic chondrosarcoma (Ewing) | 5 months..... | Three high voltage roentgen-ray treatments, June, 1923, to December, 1923 | Increase in pain and swelling; amputation, March 11, 1925 | Metastases one lung 4 months later |
| None | 6 months..... | High voltage roentgen-ray treatment for 1½ months, until Feb. 19, 1925 | Feb. 28, 1925, evidence of considerable increase in size of tumor; no evidence of metastases in lungs; May 18, considerable increase in ossification of tumor; appeared definitely encapsulated | Feb. 28, 1925, roentgenogram of chest revealed evidence of large metastatic tumors; died shortly after |
| Pain 4 months; swelling 1 month | | Two roentgen-ray treatments before coming to Memorial Hospital; roentgen-ray treatments: Jan. 26, 1925, to chest; January 31, to chest; February 4 to March 26, 7 (80 minutes each) to femur; March 27, 35 minutes; March 30, 80 minutes; March 31, 45 minutes; April 7, 80 minutes; May 27, 60 minutes; June 3, 60 minutes | Amputation early in July, 1925, as palliative measure (Dr. Verdi, New Haven); recovery from operation (Note: This patient was not treated by us but was seen in consultation) | Well 1 year later |
| Biopsy: malignant osteogenic central sarcoma (Ewing) | Few months; June, 1925, large, fungating tumor | Roentgen-ray treatment for 4 months; disease not controlled; evidence of abdominal metastases | Steady increase in size... Died | |
| Osteogenic periosteal sarcoma | 3 to 4 months..... | Radium | Steady increase in size; amputation, October, 1921 (Quick) | Reported well, October, 1924 (Dr. Quick) |
| Large, spindle cell, osteogenic sarcoma, periosteal soft chondroma; rather numerous cells, large spindle, about lobules of cartilage | 6 months pain..... | Radium pack 4 months (Dr. D. Quick), 85,000 millicurie hours | Little effect in tumor; steady increase in size | Further intensive roentgen-ray treatment after leaving Memorial Hospital; died of exhaustion July, 1923 |
| Fibro endothelioma, not essentially malignant | 3 years pain; 2 years tumor | Treated 3 years for neuritis; radium (44,864 millicurie hours) and roentgen rays (14 treatments) | Steady increase in size; amputation, October, 1921 (Quick) | In good condition, August, 1925 |
| No biopsy | 1 year..... | Radium (40,027 millicurie hours); disease not controlled; amputation, October, 1920 | Metastases in lung 5 months after amputation | Probable metastases; died July, 1920 |
| No biopsy | 6 months pain..... | Eight doses toxins; radium, 83,000 millicurie hours | No increase in tumor; 10 months later general condition good; great improvement; in 2 years; then grew worse | In hopeless condition, September, 1925; died shortly after |
| No biopsy | 6 months pain..... | Had 8 doses Coley's toxins, then treated with radium, 8 treatments (83,000 millicurie hours) | Interscapular amputation (Dr. Adair); recovery | Well, December, 1924 |
| No biopsy | 6 months pain; 4 months swelling | Local operation, July, 1923; high voltage roentgen rays, October, 1923, to January, 1924; steady increase in size; March 1, 1924, fungating tumor removed with cautery (Dr. Stone) | Recovery | |
| Metastatic sarcoma (Larkin) | Few months..... | Roentgen rays 4 months; increase in size; amputation, January, 1923 (Dr. B. L. Coley) | Recovery | |
| Spindle cell sarcoma (Larkin) | Paralysis 2½ years before | Roentgen rays; resection head of humerus, head of scapula and outer end of clavicle (Dr. N. W. Green) | Slight improvement | |
| No biopsy | Pain 6 months; tumor soon after | Roentgen-ray treatment, 9 exposures from January to March, 1922 | Well 9 years later; resection was for an old roentgen-ray burn that would not heal; discovered on microscopic examination of specimen | Not traced |

TABLE 7.—Group II: Patients Treated with

| Date | Age | Sex | Locality | Trauma | Clinical Diagnosis | Roentgen-Ray Diagnosis |
|-------------------|-----|-----|-----------------------|--|----------------------------------|----------------------------------|
| March, 1917 | 44 | ♀ | Humerus, upper end | None..... | Periosteal sarcoma | Periosteal sarcoma |
| June, 1915 | 19 | ♂ | Humerus, lower end | Fracture 2 years be- fore | Periosteal sarcoma ? | Probable sarcoma... |
| February, 1919 | 57 | ♂ | Humerus, upper end | None..... | Periosteal sarcoma | Periosteal sarcoma ? |
| February, 1919 | 19 | ♂ | Humerus, upper end | Local injury in 1918; pain and swelling soon after | Periosteal sarcoma | Periosteal sarcoma |
| November, 1921 | 15 | ♀ | Humerus, upper end | ?..... | Periosteal sarcoma | Periosteal sarcoma |
| February, 1915 | 34 | ♀ | Humerus, upper end | Local injury; pain 6 months later | Chondrosarcoma.... | Sarcoma..... |
| March, 1920 | 15 | ♂ | Humerus, middle | Recent fracture..... | ?..... | ?..... |
| October, 1921 | 13 | ♀ | Tibia..... | Local trauma..... | Periosteal sarcoma | Periosteal sarcoma |
| November, 1923 | 13 | ♂ | Tibia, upper end | Injured shin diving off springboard, August, 1923; pain 3 to 4 weeks later; tumor 2 months after injury | Periosteal sarcoma | Periosteal osteogenic sarcoma |
| June, 1922 | 57 | ♂ | Tibia, upper end | Fell downstairs, wrenching leg; tu- mor 1 week later | Periosteal sarcoma | Periosteal sarcoma |
| June, 1922 | 55 | ♀ | Tibia, upper end | Local injury, May, 1920, also June, 1920, and May, 1921; tu- mor 6 weeks after last injury | Central sarcoma, giant cell ? | Giant cell sarcoma... |
| June, 1923 | 41 | ♀ | Tibia, shaft..... | None..... | Periosteal sarcoma | Periosteal sarcoma |

Radium and Roentgen Rays—Continued

| Microscopic Diagnosis | Duration | Treatment | Immediate Result | Final Result |
|---|--|--|---|---|
| No biopsy | Pain 2 years; tumor more than 1 year | Massage and osteopathy for several months; 11 months before had radium in Baltimore | Little improvement; had huge inoperable tumor when admitted to Memorial Hospital; received palliative radium treatment | Died, Dec. 5, 1918 |
| Osteosarcoma, probably periosteal (Ewing) | Tumor 3-4 years; began to grow 9 months before examination | Local excision, February, 1918; encapsulated tumor attached to periosteum, outer condyle; prophylactic radium at Memorial Hospital (21,000 milliecurie hours), March, 1918 | ? | Not traced |
| Osteochondrosarcoma | Pain and disability following typhoid inoculation 1½ years before; treated 1 year for neuritis | Operation, Jan. 21, 1919, New York Hospital (Dr. Hitzrot); resection upper 4 inches (10.1 cm.) of bone; bone graft implanted; referred to Memorial Hospital, February, 1919 | Treated with radium pack 3 months (85,000 milliecurie hours); roentgen-ray examination, April and May, showed recurrence of disease | Gradually returned to normal; patient well, June, 1925, 6 years later |
| Osteogenic sarcoma; chondrosarcoma structure shows mostly cartilage | 6 months..... | Radium treatment (60,250 milliecurie hours) by Dr. Janeway, February and March, 1919 | Tumor steadily increased in size; very large in October, 1919, when Dr. Matthews, at St. Luke's Hospital, did interscapular thoracic amputation | Died; lung metastases 5 months later |
| Osteogenic sarcoma | 7 months..... | Treated with roentgen rays at Mt. Sinai Hospital 6 weeks after first noticed; amputation advised but refused; roentgen rays continued; admitted to Memorial Hospital November, 1924; amputation advised but refused | Palliative treatment; given; lungs free | Died few months later |
| Chondroma (February, 1918); chondrosarcoma (May, 1919) | 1 year..... | Local operation, June, 1917; amputation advised by several surgeons; treated at Memorial Hospital with radium pack (10 treatments) and bare tubes (7 treatments, 9 to 37 milliecurie hours) from Feb. 8, 1918, to Aug. 8, 1919 | Marked improvement; large tumor nearly disappeared; recurred and no longer favorably affected by resection | Died early in 1920 |
| Myxosarcoma | Few weeks..... | Operation 1 month after fracture; roentgen rays and radium (9,790 milliecurie hours), March 25, 1920 | Recovery | Well 3 years later |
| Osteogenic sarcoma (Ewing) | 2 months..... | Roentgen-ray treatment 4 weeks; amputation followed by toxins | Recovery | Metastases in lung and large recurrence in stump of thigh 8 months after amputation; condition very far advanced; huge tumor and condition regarded as hopeless when patient first came under our observation |
| Chondrosarcoma | 2 months..... | Dec. 19 to 22, 1923, 48,000 milliecurie hours radium (pack) at 10 cm. distance; Feb. 15 to 18, 2 exposures high voltage roentgen rays, 80 minutes (Dr. D. Quick) | Tumor not controlled; amputation performed, March 17, 1924 | Metastases in 2 to 3 months; died |
| Spindle cell periosteal sarcoma | 1½ years..... | Radium, 50 milliecurie hours, bare tubes in tumor Aug. 3, 1922; radium packs (78,916 milliecurie hours) from July, 1922, to Jan. 24, 1923 | Steady increase in size of tumor; amputation by Dr. B. L. Coley | |
| Gross diagnosis: telangiectatic osteogenic sarcoma, aneurysm of bone with giant cell reaction (Ewing) | 1 year..... | Radium pack (6,249 milliecurie hours), June, 1923; 13 injections toxins, June, 1922; 8 high voltage roentgen-ray treatments, June, 1922, to January, 1923 | Steady increase in size; increase in bone formation; pathologic fracture; leg useless, October, 1923, to June, 1924; amputation at thigh June 5, 1924 (Coley), followed by toxins | Well, December, 1924; August, 1926, general condition poor; no definite evidence of metastases |
| Alveolar sarcoma, periosteal | Swelling of tibia 2 years before; 2 years later local removal; local recurrence 5 years before; second local removal, April, 1922, by Dr. Parker; recurrence, July, 1922, with metastases in lungs | Roentgen-ray treatment at Memorial Hospital July, 1922, to January, 1923, 9 treatments; further treatment in 1924 | Local condition controlled; metastases in lung held quiescent for 2 years; general condition good | December, 1924, general condition good; lung metastases getting larger; April, 1926, general condition much worse |
| Structure indicates slowly growing, sclerosing type of osteogenic sarcoma | Pain 3 years; swelling soon after; no treatment until July, 1923 | Oct. 12, 1923, 1 roentgen-ray treatment | No change | In good condition, December, 1924 |

TABLE 7.—Group II: Patients Treated with

| No. | Date | Age | Sex | Locality | Trauma | Clinical Diagnosis | Roentgen-Ray Diagnosis |
|-----|-----------------|-------|-----|----------------------------|--|--|---|
| 10 | August, 1921 | 17 | ♂ | Tibia, upper shaft | None..... | Sarcoma..... | Proliferation of periosteum; medullary canal somewhat expanded |
| 11 | May, 1922 | 16 | ♂ | Tibia, upper half of shaft | None..... | Osteomyelitis; periostitis (Bloodgood); Paget's disease; subperiosteal, nonsuppurating periostitis | Osteitis or osteomyelitis |
| 12 | September, 1921 | 15 | ♂ | Tibia, shaft..... | Fall 7 months; local injury head of tibia; tumor 2 months | Osteomyelitis (Hospital for Ruptured and Crippled) | Lacks appearance usually noted in periosteal or giant cell growths; diagnosis: endothelioma (Herendeen) |
| 13 | March, 1921 | 14 | ♀ | Tibia, upper end | None..... | Central sarcoma.... | Giant cell tumor.... |
| 14 | June, 1919 | 19 | ♂ | Tibia, upper end | None..... | Central sarcoma.... | Benign giant cell sarcoma |
| 15 | November, 1919 | 14 | ♀ | Radius, shaft..... | Strain, November, 1918; swelling next day at site of injury; second injury, July, 1919; tumor next day persisted | Periosteal sarcoma | Sarcoma..... |
| 16 | May, 1919 | 19 | ♂ | Ulna, shaft..... | Frequent strain from cranking car | Periosteal sarcoma | Periosteal sarcoma |
| 17 | March, 1919 | 17 | ♂ | Radius, lower end | Sprain 4 years before; tumor soon after slowly increased in size | Periosteal sarcoma | Periosteal osteosarcoma |
| 18 | March, 1919 | 12 | ♀ | Clavicle, inner end | None..... | Periosteal sarcoma | Periosteal sarcoma |
| 19 | March, 1921 | 39 | ♀ | Clavicle, inner end | None..... | Sarcoma..... | Destructive process inner end clavicle and sixth cervical vertebra simulated endothelioma |
| 20 | October, 1922 | 9 | ♂ | Os calcis..... | None..... | Endothelioma..... | |
| 21 | 1919 | Adult | ♂ | Clavicle..... | ?..... | Sarcoma..... | Sarcoma..... |
| 22 | April, 1921 | 23 | ♀ | Tibia, upper end | None..... | Osteogenic sarcoma | Osteogenic sarcoma |
| 23 | March, 1922 | 21 | ♀ | Tibia, lower end | ?..... | Giant cell tumor.... | Giant cell tumor.... |

Radium and Roentgen Rays—Continued

| Microscopic Diagnosis | Duration | Treatment | Immediate Result | Final Result |
|--|-----------------------------------|--|--|--|
| Endothelioma (Ewing), perithelial growth in dense scar tissue | Pain 1 year; swelling 1 month | Radium pack, December, 1920, to May, 1923 (101,181 millicurie hours), also roentgen-ray treatments | Improvement; disease controlled for nearly 3 years, then signs of activity; amputation, November, 1923 | Well 1 year later |
| No biopsy; chondrosarcoma (Ewing) | 4 months, severe constant pain | Removal of teeth; roentgen-ray treatment, May, 1922; amputation at thigh, August, 1923 | Pain and disability increased and became very severe | Died of lung metastases 2 months later |
| No biopsy | Pain 5 months; swelling later | Roentgen rays, September to December, 1922, 6 treatments (Herendeen) | Marked improvement | Well, December, 1924 |
| Giant cell tumors, epulis type | 4 months..... | Curettage, New York Hospital, October, 1920; second operation, March, 1921; 32 millicurie hours bare tubes and 222 millicurie hours silver tubes radium; several radium pack and bare tube treatments at Memorial Hospital | Disease not controlled; amputation at Presbyterian Hospital, October, 1921; recurrence in thigh stump 6 months later | Further roentgen-ray treatments; died in 1922 of extension of metastases in pelvis |
| Benign giant cell sarcoma (Ewing, Bloodgood, Malory, Codman); osteogenic sarcoma with giant cells, malignant (Wood) | 5 months pain..... | Curettage, Dr. Walton Martin, June, 1919; referred to Memorial Hospital after operation, June 28, 1919; treated with radium, bare tubes (2,256 millicurie hours) unfiltered radium | Cavity slow in healing but no infection until April, 1920, when recurrence was noticed; second curettage infection; amputation (Coley), June 9, 1920 | Developed metastases in both lungs, February, 1921; died 2 months later |
| Endothelioma; endothelial myeloma (Ewing) | 4 months..... | Small doses of toxins at Mt. Sinai Hospital for 2 weeks; admitted to Memorial Hospital Nov. 25, 1919; radium, December to November, 1920 (11,238 millicurie hours), pack at 6 cm. distance | Almost complete disappearance of tumor in few weeks; August, 1920, arm normal; September, 1920, recurrence; metastases rapidly developed | Died, January, 1921; much emaciated; skull studded with tumors |
| Osteogenic sarcoma | Few months..... | Radium at Memorial Hospital (Dr. D. Quick) from May to October, 1919 | Steady increase in size; amputation at St. Luke's Hospital (Dr. Schley), Oct. 27, 1919 | Metastases 3 months later; died |
| "Sarcoma" (at another hospital) | 4 years..... | Excision 3 months before at another hospital; local recurrence; treated with radium at Memorial Hospital (Dr. Jane-way) 18,918 millicurie hours at 3 cm. distance in lead plaques, 3 mm. lead filter | Superficial burns; little effect on tumor; amputation advised | Returned to Italy; not traced |
| No biopsy | 1 month..... | Radium pack (30,156 millicurie hours), radium bare tubes (17 millicurie) by Dr. D. Quick; 7 roentgen-ray treatments | Marked improvement; tumor nearly disappeared; recurrence in 3 months | Died Jan. 20, 1920; total duration of disease, 6 months |
| Small, round, polyhedral cells show features of endothelial cells but not typical of endothelioma, may be myeloma or epithelioma | 9 months..... | Radium (32,670 millicurie hours) at 6 cm. distance | Recovered from paralysis; tumor disappeared | Well 2 years; death, June, 1925, possibly due to metastases |
| Endothelioma | 1 year..... | Radium (48,000 millicurie hours) at 6 cm. distance; roentgen rays from Oct. 3, 1923, to May 6, 1924 | Some improvement; later pain and swelling increased; metastases | Died, May 14, 1924 |
| Myeloma | | Excision of clavicle by Dr. Hitzrot at New York Hospital; local recurrence | Treated at Memorial Hospital with radium (Dr. Quick); disease not controlled | Died 6 months later from what we believe to be lung metastases |
| No biopsy | 4 months..... | Roentgen-ray treatment at Memorial Hospital (Herendeen) | Steady but slow increase in size, increased more rapidly last few weeks; very much new bone production | Under treatment |
| No biopsy | Swelling immediately after injury | Roentgen-ray treatment at Memorial Hospital from April 20 to Sept. 20, 1925 | Condition gradually getting worse | Metastases in lungs, September, 1925 |

* In this table, ♂ indicates male; ♀, female.

thirty-nine years later. Of these thirty-eight patients, twenty were treated with toxins alone (the limb saved in eight cases) and eighteen were treated with toxins and radium (the limb saved in eleven cases).

TABLE 8.—*Patients with Periosteal Osteogenic Sarcoma, Including Endothelioma, Well Five Years Plus*

| Case | Locality | Treatment | Results |
|------|---|--|--|
| 1 | Tibia..... | Toxins alone..... | Well 27 years; limb saved |
| 2 | Humerus..... | Toxins alone..... | Well 24 years; limb saved |
| 3 | Femur..... | Toxins alone for extensive metastases after failure of roentgen rays | Well 11 years; limb saved |
| 4 | Femur..... | Amputation and toxins..... | Well 17 years |
| 5 | Femur..... | Amputation and toxins..... | Well 16 years |
| 6 | Humerus..... | Toxins, amputation, toxins..... | Well 8 years; then died of lung metastases |
| 7 | Femur..... | Toxins alone..... | Well 12 years; limb saved |
| 8 | Femur..... | Toxins and radium..... | Well 5 years; limb saved |
| 9 | Femur..... | Toxins alone..... | Well 13 years; limb saved |
| 10 | Humerus..... | Toxins and roentgen rays..... | Well 15 years; limb saved |
| 11 | Tibia..... | Toxins and radium (clinical and roentgen-ray diagnosis) | Well 6 years; limb saved |
| 12 | Femur (inoperable) | Toxins and radium..... | Well 8 years; limb saved |
| 13 | Clavicle..... | Excision and toxins..... | Well 15 years |
| 14 | Clavicle..... | Excision and toxins..... | Well 16 years |
| 15 | Femur..... | Toxins, radium, amputation, toxins six months | Well 8 years |
| 16 | Femur..... | Radium, toxins, amputations, toxins..... | Well 8 years |
| 17 | Tibia..... | Amputation and toxins..... | Well 8 years |
| 18 | Femur..... | Toxins, radium, amputation, toxins..... | Well 5½ years |
| 19 | Metatarsal bone | Amputation; recurrence; toxins..... | Well 30 years |
| 20 | Metatarsal bone | Amputation and toxins..... | Well 12 years |
| 21 | Femur..... | Toxins, amputation, toxins..... | |
| 22 | Radius..... | Roentgen rays, toxins, amputation, toxins | Well 16 years Well 13 years |
| 23 | Mastoid..... | (Four recurrences.) Radium; failure to control; toxins | Well 9 years |
| 24 | Rib..... | Toxins (clinical and roentgen-ray diagnosis) | Well 9½ years |
| 25 | Tibia with metastases in inguinal, iliac and femoral glands | Radium and toxins (2¼ years)..... | Well 9½ years |
| 26 | Femur..... | Toxins, radium, amputation, toxins.... | Well 9 years |
| 27 | Femur..... | Amputation and toxins..... | Well 18 years |
| 28 | Femur (inoperable); metastases in skull | Toxins and radium..... | Well 6¾ years |
| 29 | Fibula (inoperable); metastases in groin and lungs | Toxins 3 months; 1 radium treatment to groin | Well 5¼ years |
| 30 | Humerus (inoperable) | Toxins | Well 7 years; limb saved |
| 31 | Femur..... | Toxins | Well 6 years; limb saved |
| 32 | Femur (roentgen-ray and clinical diagnosis) | Toxins | Well 5 years |

Limb saved in 15 cases

Microscopic examination in 26 cases (periosteal osteogenic sarcoma, 20 cases; endothelioma, 6 cases).

Cases in Which Clinical and Roentgen-Ray Diagnosis Was Made

- 1 Exploratory incision; typical periosteal sarcoma of femur
- 2 Beyond hip joint amputation; destruction of 5½ inches (13.9 cm.) of femur
- 3 Packard's case; inoperable, upper third of femur; child weak and emaciated when treatment was begun
- 4 Roentgen-ray and clinical diagnosis; probable endothelioma of tibia
- 5 Inoperable first rib; clinical and roentgen-ray diagnosis; sarcoma
- 6 Inoperable sarcoma of humerus, with metastases in lung

* Williamson's case. † Mackie's case. ‡ Willmoth's case. § Packard's case.

CONCLUSIONS

1. The prognosis of osteogenic sarcoma of the long bones, while far from satisfactory, is by no means as hopeless as is generally believed by physicians.

2. The prognosis depends largely on an early diagnosis and the exercise of most careful judgment in selecting the method of treatment for the individual cases; this should be based on a wide experience with a great variety of clinical and pathologic types of bone sarcoma.

3. Amputation alone offers little hope of a permanent cure in any of these types.

4. Primary treatment with radium or roentgen rays, even if pushed to the utmost limits of safety, while often causing very marked improvement has thus far failed to effect a permanent cure in any case in which the diagnosis has been unquestionably established by clinical and pathologic evidence.

5. The mixed toxins of erysipelas and *Bacillus prodigiosus* alone have effected a cure in a certain number of cases; but all of these cases have been of the round cell or spindle cell type, characterized by little production of new bone.

6. The mixed toxins and radium combined have likewise resulted in the complete disappearance and apparent cure of an even larger number of cases of a similar type; but neither toxins nor radium, singly or combined, have effected a cure in any case associated with marked new bone production.

7. Amputation followed by prolonged treatment with the mixed toxins in a series of thirty-eight consecutive cases shows 50 per cent of the patients alive and well from three to eighteen years. This series includes all types of osteogenic sarcoma, as well as the cases associated with marked new bone formation.

8. In a similar series of cases treated by amputation alone without toxins or radium before or after amputation, not a single patient has remained alive beyond the three year period.

9. The choice of treatment in a given case depends on whether it belongs to the group of round cell sarcoma (endothelioma, according to Ewing's classification) or to the group associated with marked new bone formation. If to the first group, we believe it is safe to try a combination of the systemic effect of toxins and the local effect of radium, the duration of the treatment to depend on the result obtained; if marked improvement is noted, the treatment may be continued until the tumor has entirely disappeared; but if no improvement is noted in from four to six weeks amputation should be performed, followed by prolonged systemic toxin treatment.

If the case belongs in the second group, we see no advantage, but a distinct disadvantage, in preliminary treatment with radium, roentgen rays or toxins, for the reason that metastases may develop during the period of treatment or may be hastened by the rapid breaking down of a vascular tumor, which permits living cells to be carried to the lungs

or to remote parts of the body. As our experience, supported by the results of other men, shows that there is no reasonable hope of saving the limb in this group of cases, we believe that amputation at the earliest possible moment followed by prophylactic toxin treatment offers the greatest hope of saving the life of the patient.

10. The fact that ten inoperable cases of this series have been successfully treated with the mixed toxins alone or combined with radium, the patients remaining well from five to twenty-four years later, should prevent us from abandoning all hope in cases beyond surgical relief.

(To be continued)

TOTAL COLECTOMY AS A TREATMENT OF THE MEGASIGMOID; END-TO-SIDE ANASTOMOSIS *

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In a series of twenty-five partial resections of the sigmoid flexure (megasisigmoid) including nine complicated cases,¹ I have noted during a period of from six months to two years a relapse in one fourth of the cases. Judging from this result, I conclude that in my hands partial colectomy for this condition has not been successful.

This failure may not cause any surprise because by means of the partial colectomy only the most altered portion of the colon is removed. The supralying and the infralying segments may transform themselves, in time, to an inert receptacle for feces. My attention was duly called to the fact that the recurrences among the noncomplicated cases with an emergency condition were noted in those cases in which a clinical picture of a left sided constipation predominated. Among the complicated cases, 50 per cent repeated "fecalomas" were registered in the history. The four reported patients with volvulus who had the sigmoid removed were cured permanently.

With this experience I decided to treat the left sided constipation, chiefly complicated in the fecaloma and when all treatments have failed, by means of total colectomy.

REPORT OF CASES

CASE 1.—*History*.—M. C. N., a woman, aged 27, married, a cook, was admitted to the surgical ward of the hospital de clinicas, Aug. 23, 1911. She had had five children. From her childhood she had been constipated. Toward the middle of 1921 a large fecaloma was removed from her.

Since some fifteen days before admission she had been unable to move her bowels even with purgative or enema. During the last few days she had complained from time to time of sharp abdominal pains. Gas was passed only with difficulty.

Physical Examination.—There was pronounced abdominal meteorism. Peristaltic waves were visible through the abdominal wall. By palpation a tumor the size of the head of a fetus could be felt over the pubis; it was embedded in the superior strait of the pelvis, of a pasty substance and pliable to pressure with the fingers.

The palpation of the abdomen was painful. It was found that the fecaloma occupied part of the pelvic cavity.

* From the surgical department of University of Cordova Medical School.

1. Mirizzi: Colectomia de urgencia por megacolon ileo-pelviano complicado, Rev. Asoc. méd. argent., September, 1921, No. 203.

August 24, oil, soap and oxygenated water enemas were tried without any result whatever. There was vomiting and abdominal pain. The pulse, respirations and temperature were normal. The fecaloma had not changed.

August 25, an attempt was made to extricate the fecal accumulation with the hand, but it could not be reached. The general condition of the patient remained unchanged.

Operation.—August 26, a total colectomy² was performed, Dr. F. Olmedo assisting me. The operation lasted two hours and fifteen minutes. The first hour

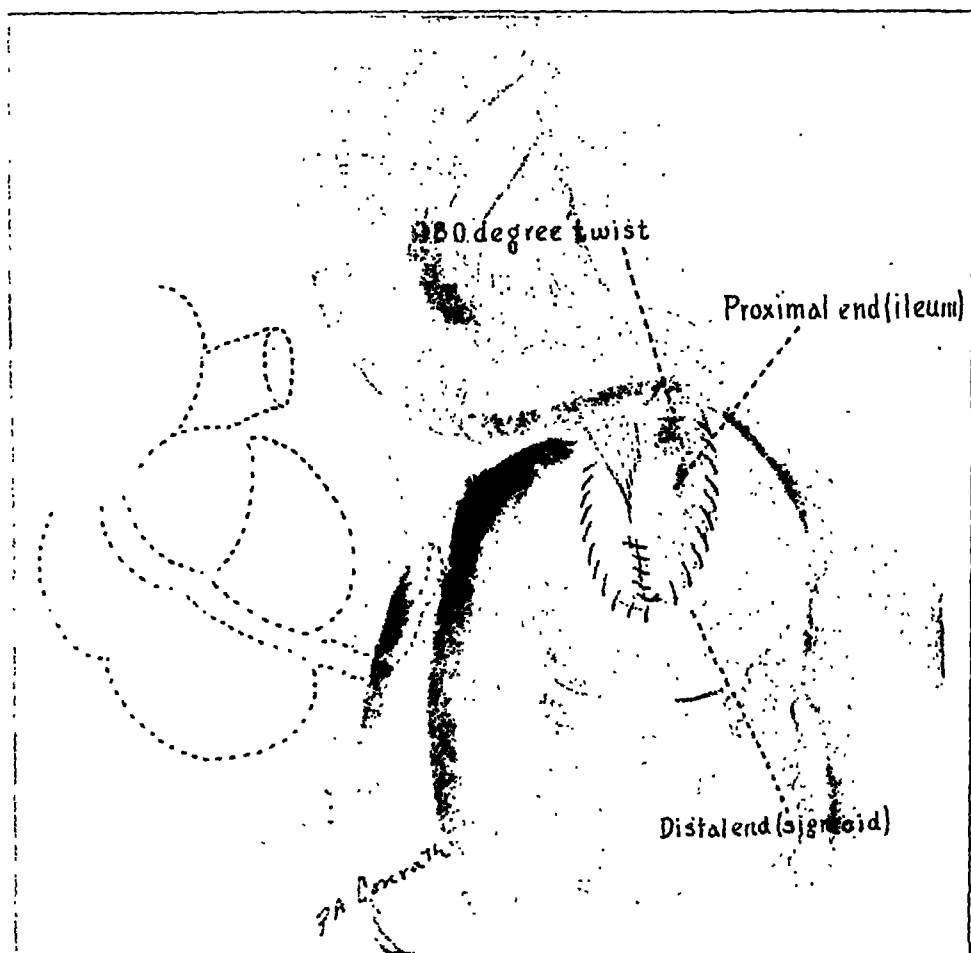


Fig. 1.—Side (of ileum) to end (of sigmoid) anastomosis, showing forward concavity and undesirable twist of 180 degrees.

and a quarter spinal anesthesia with stovaine-strychnine (Jonnesco) was used; the remaining forty-five minutes were under general anesthesia with ether, chloroform and oxygen (Roth-Drager apparatus).

A midline incision, 4 inches (10.1 cm.) above and below the umbilicus, was made. An enormous sigmoid flexure with a large amount of fecal contents was easily brought out. The operation was carried on by a careful separation of the

2. Strictly speaking, a total colectomy never is carried out owing to the fact that the anus, rectum and a few inches of the distal sigmoid flexure are left in place.

omentum from the transverse mesocolon (Lardennois-Okinczyc); easy loosening of the right and left colic angles, ascending, descending and sigmoid flexure. The hemostasis was easily accomplished by six ligations. The ileum was cut 5 cm. from the Bauhin valve with the cautery; the sigmoid was cut a few inches above the rectum with the scalpel and the end was touched with 5 per cent tincture of iodine. The end of the ileum was closed according to the De Martel procedure. A side opening was made in the ileum (9 cm.) in order to make an anastomosis with the colon (side-to-end anastomosis). The end of the ileum brought in contact with the distal opening³ described a forward concavity. Near the anastomosis was noted a twisting of the ileum of 180 degrees around its longitudinal axis (fig. 1). In view of the obstruction caused by this abnormal location of the ileum, the anastomosis was undone, being fixed in the manner indicated in the paragraph relating to the technic of so-called side-to-side anastomosis, that is to say, with the loop of the ileum describing an anterior convexity. By doing this the proximal portion was drawn in contact with the posterior border (mesosigmoid) of the distal portion (fig. 2). Waxed linen thread was used in three rows of continuous sutures. Drainage through the anastomosis with a Faucher rubber tube was established through the anus.

The postoperative period was quiet and the patient made an uneventful recovery, leaving the hospital twenty days later.

This patient was examined in January, 1925, and was pregnant and perfectly well, having three or four stools daily. Lately, I learned that she gave birth to her child and is enjoying good health.

CASE 2.—History.—A. S., a married woman, aged 26, an Argentinian, entered the surgical ward of the hospital de clinicas, Sept. 14, 1922.

She had had whooping cough, smallpox and measles during childhood, and constipation for the last ten years. Lately two fecalomas were extracted.

Since one month before admission she had not been able to move her bowels, either with purgative or with enemas; she suffered general discomfort and sometimes sharp pain in the abdomen.

Physical Examination.—Information obtained by abdominal and rectal examinations demonstrated an enormous amount of feces in the distal portion of the colon. During the days following her admission the colon was emptied by means of enemas and manually.

Operation.—September 23, I performed a total colectomy, Dr. F. Olmedo assisting me. The operation lasted two hours under general anesthesia with ether, chloroform and oxygen (Roth-Drager apparatus). A midline incision was made. The easy separation of the transverse mesocolon from the omentum, as described by Lardennois and Okinczyc, was this time difficult; the left colic angle was troublesome to detach; hemostasis was obtained with five ligations; the ileum was cut 5 cm. above the Bauhin's valve by cautery; the sigmoid flexure was separated as near as possible to the rectum with the scalpel and immediate application of 5 per cent tincture of iodine was made.⁴ The proximal end (ileum) was stitched up according to De Martel. Anastomosis was accomplished with three rows of continuous suture, using waxed linen thread. The anastomosis was made as shown in figure 2, and rubber tube drainage was instituted through the anastomosis.

3. For a better understanding, the end of the ileum and its lateral opening will be called proximal and the end of the sigmoid will be called distal.

4. The diameter of the distal opening (colon) measured 10 cm.

Fig. 2.—Side (of ileum) to end (of sigmoid) anastomosis, showing anterior convexity which is the position desired to avoid the twist of 180 degrees.

whooping cough and measles between 5 and 9 years of age, and had had constipation from childhood. On admission she had had no stool for a month.

Physical Examination.—She had chronic bronchitis and metrorrhoea. At the clinic it was noted that the sigmoid flexure and the rectum were the seat of a large fecaloma. During the following days by enemata and manually the colon was emptied.

Operation.—November 30, as the patient was in fairly good general condition, I operated, assisted by Dr. F. Olmedo. Chloroform anesthesia was used. A midline

incision was made above and below the umbilicus. The dissection of Lardennois and Okinczyc was impossible; the detachment of the colic angles was easy. The ileum was cut 5 cm. above the Bauhin's valve with cautery. The incision of the colon was made with the scalpel as near as possible to the rectum, followed by application of 5 per cent tincture of iodine. The distal opening was 8 cm. in diameter. The end of the ileum was closed. Side-to-end anastomosis between the ileum and the sigmoid was made. When the anastomosis was finished the patient died of heart syncope.⁵

CASE 4.—History.—J. S., a workman, aged 42, was admitted to the hospital de clinicas, July 15, 1924. He had measles during childhood, and complained of chronic intestinal stasis for twenty years. He had tried several treatments but poor results were obtained. The year before this admission he came to the hospital and a fecaloma was removed.

Present Illness.—He complained of being unable by all means tried to move his bowels, and stated that from time to time he had abdominal pain. When a certain amount of gas was eliminated the pains were not so frequent nor so severe. Purgatives and enemas had entirely failed. At the hospital, after previous anal dilatation, the fecaloma was taken out.

Operation.—A few days afterward when the patient was in better condition and the colon was partially emptied, the operation was performed, Dr. F. Olmedo assisting me. Spinal anesthesia was used (0.1 procaine). The operation lasted one hour and forty-five minutes. A midline laparotomy was done. The sigmoid flexure had attained a gigantic size and the remainder of the colon was larger than normal. The left colic angle was surrounded by strong and old adhesions. The separation of Lardennois and Okinczyc was possible. The total resection of the colon was easy, except for the left angle. The colic arteries were individually ligated. The ileum was cut 5 cm. above the Bauhin's valve, and closure of the proximal end was made by De Martel's method. The sigmoid flexure was cut as far down as possible. The distal opening (10 cm.) was three times wider than the lumen of the ileum. The anastomosis was made following the plan shown in figure 2 (anterior convexity of the ileum), using waxed linen in the three rows of continuous stitches. Intestinal drainage was instituted through the anastomosis by means of a rubber tube.

The patient made an uneventful recovery and left the hospital twenty days afterward perfectly well.

Two months later he came again with a small fecal fistula located in the lower third of the operative scar. He said that ten days before he had noticed a painful spot on the lower abdomen, which gave place afterward to a swollen area. The latter broke down, discharging a certain amount of gas and intestinal contents, after which he had immediate relief.

It seemed probable that the unabsorbable material was the cause of the fistula. Under local anesthesia, avoiding the peritoneal cavity, I enlarged the fistulous tract, removing two pieces of waxed linen which were floating in the intestinal lumen.

The patient left one month later, relieved of the fistula and moving his bowels three times a day.

One year later he was reported to be in good health.

5. The chloroform was doubtless the main factor.

If the difficulties are considered which one has to overcome in making a total colectomy where there is a megasigmoid flexure, one of them is doubtless the enormous size of the distal opening (sigmoid). To my mind this is the most serious difficulty; even with a folding of it⁶ helped by a great elasticity of the ileum, it would be impossible to make an end-to-end anastomosis. Three ways can be followed to obviate the inconvenience: (a) an end-to-end anastomosis without folds, similar to the Billroth I between the stomach and the duodenum; (b) end (ileum) to side (sigmoid) anastomosis, and (c) side (ileum) to end (sigmoid) anastomosis.

I have preferred the third variety, which, in my judgment is free from the inconveniences of the other two. The possibility of leakage at the junction of the three suture lines in the first procedure and the making of a side opening through a somewhat altered intestinal wall (rectum and sigmoid) in the second method, seems to be undesirable.

TECHNIC OF THE SIDE-TO-END ANASTOMOSIS

In side-to-end anastomosis the end of the ileum should be closed, preferably using De Martel's procedure. Before approximating both portions it is necessary to carry all the small intestine toward the upper part of the abdomen. The proximal portion is drawn backward until it lies beside the remaining mesentery of the sigmoid flexure. The ileum describes when it is placed correctly "an anterior convexity," as can be seen in figure 2. The side opening (ileum) is made opposite the border of the mesenteric attachment and begins 2 cm. from De Martel's closure and should be as long as the distal opening (sigmoid).

I suggest in regard to the material that should be used for the anastomosis that it is preferable to employ chromic catgut 00 rather than linen to avoid the possibility of an intestinal fistula (case 4).

The first row (outer line) is seroserosa; the second line of continuous suture (middle row) goes through the seromuscular coats and the third row (inner line) stitches both mucous coats along the first half. All the coats are brought together during the second half. After finishing the three concentric suture lines the proximal end is fixed posteriorly.

Finally, the window between the mesentery and the mesocolon should be closed with a continuous suture.

Indispensable Precautions.—There is a natural tendency to perform the anastomosis in the wrong way (fig. 1). I wish to recall that in describing case 1 I stated that on finishing the anastomosis the ileum presented a twist of 180 degrees around its longitudinal axis. The

⁶ Hirsch-Arana: Técnica de la colectomía, *Semana méd.*, June 14, 1917.

anastomosis was undone and made as is shown in figure 2. When we proceeded in this way no twist was observed.

Causes of the Twist of the Ileum.—If we judge by the observation in case 1 and by dissections in the necropsy room, an important cause of the twist of the ileum is the divergent attachment of the mesentery of the ileum and of the mesosigmoid flexure on the posterior abdominal wall; the former holds and pulls the ileum to the right and the latter to the left or at least fixes the lower portions of the sigmoid flexure in the midline (fig. 3).

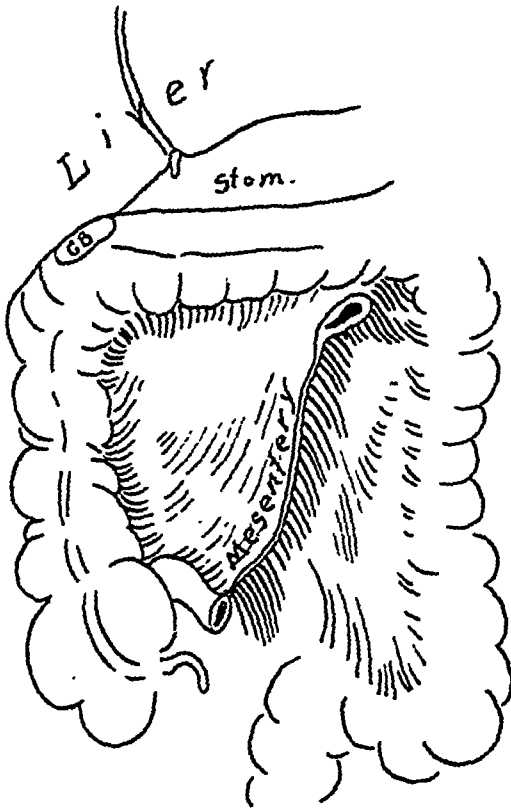


Fig. 3.—Attachment of mesentery, to show pull exerted on ileum in the production of the undesirable twist.

If the operation is carried out following the plan presented in figure 1, it follows that the portion of the ileum in which the side opening is made is twisted clockwise when the last rows of suture line are being made. The attachment of the mesentery (fig. 3) at any rate prevents the adjacent ileum following the clockwise twist, and is likely to produce opposite rotation when the mesentery is very short.⁷ In the necropsy room I had no chance to find a body with a megasigmoid flexure; therefore, I was unable to draw any conclusion. But it seems to me evident

7. The Spanish anatomist, P. Aras, who is at present teaching at Cordova Medical School, states that the shortness of the mesentery is perhaps the most important factor.

that with a normal sigmoid flexure a certain degree of adaptation, owing to its soft and thin wall, diminishes the obstructive rotation.

Result of an Intestinal Obstruction Caused by a Twist of 180 Degrees.—A rotation of 180 degrees around the intestinal axis has killed a dog. An unexpected chance provided me an interesting experience when I submitted several dogs to the method suggested by Thorn-

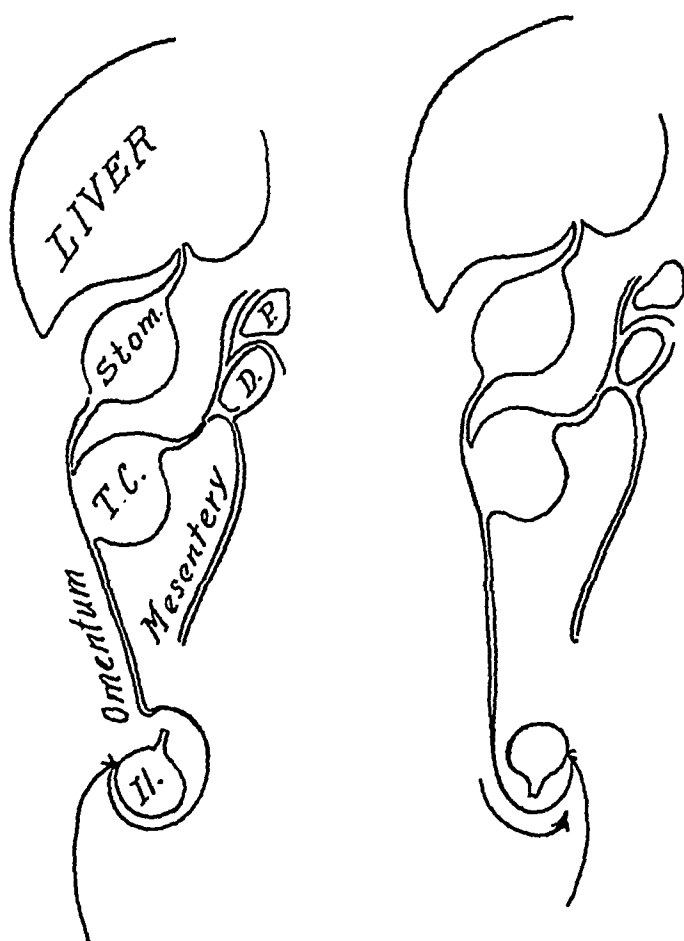


Fig. 4.—Left: portion of ileum detached from mesenteric vessels and wrapped in omentum; right: mechanism of twist of ileum.

burg and Moskowicz³ with the purpose of testing its value. The following is the observation:

Dog 2 was operated on, Jan. 29, 1922, at 11 a. m. Ten centimeters of small intestine (ileum) was detached from its mesentery. The intestinal loop became pale and shrunken; the peritoneum lost its brightness. The portion disconnected from the mesenteric vessels was wrapped up with omentum as can be seen on the anteroposterior cross section, figure 4, left.

3. Thornburg and Moskowicz, quoted by Ochsner: *Surgical Diagnosis* 3:27.

January 30 and 31, the dog was vomiting a good deal and appeared exhausted; at four o'clock, January 31, the animal died.

Postmortem Examination.—The peritoneal cavity was free from any fluid. The specimen was carefully removed and it was only found that the detached intestine had twisted 180 degrees around its axis; the rotated loop showed neither adhesions with the omentum nor necrotic points. The afferent intestine of size twice larger than normal had a cyanotic aspect and was free from either fluid contents or necrotic spots. The efferent portion had a normal aspect and was empty.

The dog died of an intestinal obstruction. The 180 degrees twist was caused by the weight of the omentum and the normal standing position of the dog (fig. 4, right). This observation shows the fatal result of such intestinal obstruction.

although locally malignant and in a few instances actually metastasizing, apparently does belong to the giant cell tumor group.

The history of the giant cell tumor is interesting in that practically all contributions on the subject include references to giant cell tumors that have been atypical and malignant. Paget⁴ in 1854, describing and referring to the condition as myeloid tumor, called attention to the general innocent nature of the tumor, but recognized that an occasional growth, apparently similar, often ran a malignant course. Nélaton,⁵ a few years later, classically described the characteristics of the tumor both clinically and histologically, but noted that atypical cases, which presented an increase in the proportion of spindle cells that became malignant. Gross⁶ in 1879 differentiated between, on the one hand, the typical giant cell tumor, a spherical growth enclosed in an osteomembranous capsule, usually occurring in the spongy substance of the epiphysis, red to maroon and of spongy and jelly-like consistency, resembling exuberant, vascular granulation tissue and containing no vestige of the original bone, and, on the other hand, a confusing malignant tumor, generally similar but lighter in color and with multiple foci of calcification and ossification throughout its substance.

More recently Bloodgood's⁷ contributions have been largely responsible for the present day attitude of the benign nature of the giant cell tumor held by many surgeons and pathologists. In a study of 177 cases over a period of thirty-two years, he has not observed metastasis, despite recurrence in some twenty-four instances, and 100 of these were well three to thirty years after operation. Codman⁸ regards giant cell tumor as a benign mass of granulation tissue and affirms Bloodgood's findings; Martland⁹ also emphasizes the benign nature of the lesion, and believes that it is an inflammatory process and a phase of osteitis fibrosa cystica. Meyerding¹⁰ studied twenty-four cases of giant cell tumor, fifteen of

4. Paget, James: *Lectures on Surgical Pathology*, Philadelphia, Lindsay and Blakiston, 1854, lecture 28, part 1, p. 446.

5. Nélaton, E.: *D'une nouvelle espèce de tumeurs benignes des os, ou tumeurs à myéloplaxes*, Paris, 1860.

6. Gross, S. W.: *Sarcoma of Long Bones*, *Am. J. M. Sc.* **78**:17, 1879.

7. Bloodgood, J. C.: *Bone Tumors*, *Ann. Surg.* **69**:345 (April) 1919; *Benign Giant Cell Tumor of Bone, Its Diagnosis and Conservative Treatment*, *Am. J. Surg.* **37**:105 (May) 1923; *The Giant Cell Tumor of Bone and the Specter of the Metastasizing Giant Cell Tumor*, *Surg. Gynec. Obst.* **38**:784 (June) 1924.

8. Codman, E. A.: *The Nomenclature Used by the Registry of Bone Sarcoma*, *Am. J. Roentgenol.* **13**:105 (Feb.) 1925.

9. Martland, H. S.: *Primary Bone Tumors: Their Classification with Special Reference to Benign Giant Cell Tumor*, *Proc. New York Path. Soc.* **21**: 102, 1921.

10. Meyerding, H. W.: *Benign Foreign Body Giant Cell Tumors in the Long Bones*, *J. A. M. A.* **83**:1323 (Oct.) 1924.

which were treated by primary curettage, five by amputation, three by resection and one by excision, and, although five of these were in turn treated by secondary amputation following recurrence and infection, he found no instance of true malignancy and concluded that they were benign lesions of inflammatory origin containing foreign body giant cells.

On the other hand, many present day students do not consider giant cell tumors altogether benign. Stewart,¹¹ in an analysis of fifty cases, found no evidence of dissemination, but because of the likelihood of recurrence regarded the tumor as a true neoplasm and as locally malignant. Stone and Ewing,¹² in a critical review of the literature, were able to find no proved instance of a giant cell tumor having metastasized but reported a case of giant cell tumor of the tibia which, following repeated curettage, infection and irradiation, changed into a large spindle cell sarcoma without giant cells and caused death from pulmonary metastasis. MacGuire and McWhorter,¹³ in a study of twenty cases, found that following treatment there was no recurrence in twelve instances, but that of the remaining eight cases, seven recurred locally, two of which metastasized to the lungs, one to the inguinal glands and abdomen, and one massively involved an amputation stump. Coley's¹⁴ review of fifty cases showed that thirty-two of the patients were well without signs of recurrence as an end-result of treatment, and that ten had died from metastasis, and, in considering the various cases of alleged malignancy reported in the literature, concluded that it was difficult to explain matters on the assumption of mistaken diagnoses in all instances. Kolodny¹⁵ cites four cases, one of which gave pulmonary metastases without giant cells, and intimates that the pendulum is swinging backward, reaffirming views formerly held regarding the relative malignancy of giant cell tumor.

The following cases, recently studied, illustrate the features of the typical giant cell tumor, essentially benign at one end of the series and relatively locally malignant at the other, but possessing anywhere along the scale the inherent power of becoming essentially a malignant tumor which, under proper stimuli, may rarely assert itself. A true sarcoma,

11. Stewart, M. J.: Observations on Myeloid Sarcoma with an Analysis of Fifty Cases, *Lancet* 2:1236 (Nov.) 1914.

12. Stone, W. S., and Ewing, J.: An Unusual Alteration in the Natural History of a Giant Cell Tumor of Bone, *Arch. Surg.* 7:280 (Sept.) 1923.

13. MacGuire, C. J., and McWhorter, J. E.: Sarcoma of Bone; An Analysis of Fifty Cases, *Arch. Surg.* 9:560-584 (Nov.) 1924.

14. Coley, W. B.: Prognosis in Giant Cell Sarcoma of Long Bones, *Ann. Surg.* 79:321 (March) 1924.

15. Kolodny, A.: Diagnosis and Prognosis of Bone Sarcoma, *J. Bone & Joint Surg.* 7:936 (Oct.) 1925.

secondarily containing giant cells of the epulis type, is cited as an example of the central bone tumor which, we feel, is often incorrectly diagnosed as benign giant cell tumor, and is largely responsible for the confusion that exists. I am indebted to the surgeons mentioned for the clinical data used in this study.

REPORT OF CASES

CASE 1.—*History*.—W. H., a white patrolman, aged 31, entered the Philadelphia General Hospital, Feb. 28, 1922, in the service of Dr. Hubley B. Owen, with the

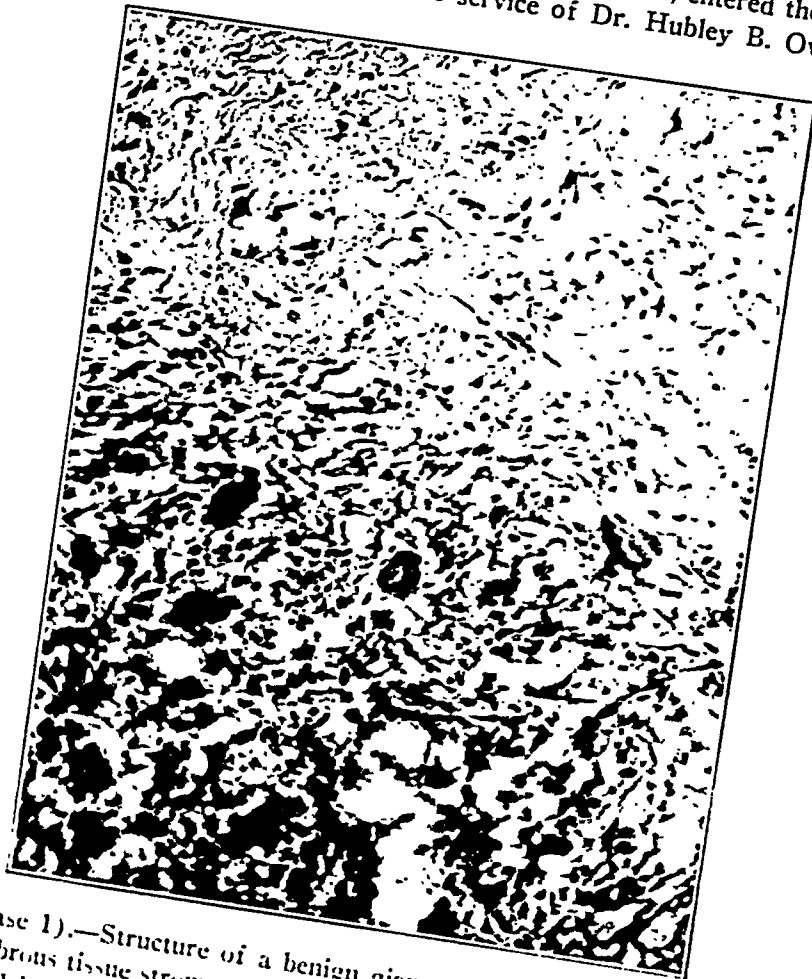


Fig. 1 (case 1).—Structure of a benign giant cell tumor well down the scale; dense adult fibrous tissue stroma, relatively acellular above but composed of mature fibroblasts and infiltrated with lymphoid cells below; several multinucleated osteoclasts, or giant cells of the epulis type, are seen in the more cellular areas; $\times 275$.

History that one year previously he had fallen, striking the right leg below the knee. For four days he was unable to walk. He recovered and returned to work but noticed sharp pains in the region of the injury "off and on." Four months ago, and again two months ago, he fell, each time injuring the right knee. He noticed slight enlargement of the knee after the second fall, and at times it was red and hot. For the last four months he had been unable to work and on admission walked with the aid of a crutch.

On physical examination there was slight swelling immediately below the right knee, apparently involving the head of the tibia. This swelling was irregular in outline, not tender to pressure, and was neither red nor hot. The other physical findings were of no consequence. The laboratory examinations were negative, and a roentgenogram taken March 1 showed "bone expanded in the head of the tibia; cortex thinned, but intact; bone rarefied, with trabeculae running through this area, giving it a multilocular, cystic appearance."

A diagnosis of giant cell sarcoma was made and, March 7, the tumor was removed by Dr. Owen by curettement to healthy bone. Convalescence was uneventful. The incision healed well. A cast was applied; the patient used crutches for six months and when seen in April, 1926, was on active patrol duty with no complaint of any kind.

Pathologic Examination.—The gross specimen consisted of many small irregular pieces of friable tissues, each having a layer of white, lusterless, dense tissue, to which were attached soft, spongy, dark reddish granulations, all intermingled with blood clot. Microscopically, the stroma was an ill-defined, loose, fibrous meshwork, moderately well infiltrated with small, rounded lymphoid and larger polygon shaped mononuclear cells in places, and was of fairly dense, wavy, hyalo-fibrous character, practically acellular, in others (fig. 1). Here and there small patches of large giant cells with abundant, opaque, acidophil cytoplasm, and containing numerous, small, oval nuclei centrally placed were noted. Spindle cells or active cells of any kind were not demonstrated; the striking feature, histologically, was the relatively acellular adult fibrous stroma, which suggested that the growth was of extremely benign nature.

CASE 2.—History.—E. G., a white married woman, aged 23, came to the Radiological Clinic of the Philadelphia General Hospital, April 21, 1926, with the history that three months previously she had turned her right ankle while walking. One month later she first noticed pain in the right knee, laterally. This pain was dull in character and was especially marked on walking or when the knee was pressed on. Swelling was never noticed. The condition became progressively worse, and during the two weeks prior to admission the knee often gave way when she was walking. No history of injury was elicited. Because of a congenital dislocation of the right hip, she had always limped; this had not increased because of the knee condition.

On physical examination there was definite fulness of the lower lateral half of the right knee, and on palpation there was tenderness immediately over the epiphysis of the fibula. The knee was stiff on passive motion, but function was not greatly disturbed. The right leg was 2 inches (5 cm.) shorter than the left because of the hip dislocation. The other physical findings were unimportant, and the routine laboratory examinations were negative.

Roentgen-ray examination revealed an expanded, rarefied, well circumscribed area involving all the head of the fibula, a picture typical of giant cell tumor (fig. 2).

April 22, Dr. J. B. Carnett resected the upper 3 inches (7.6 cm.) of the fibula, removing the growth intact. Convalescence was uneventful. The incision healed by first intention, and the patient was discharged from the hospital, May 10, in excellent general condition.

Pathologic Examination.—The head of the fibula was replaced by a solid, easily pliable tumor, ovoid in shape, and measuring 4.5 by 3.5 by 3 cm. The wall limiting the growth was everywhere intact, and was continuous with the periosteum of the fibula. It contained several small, flat, bony plaques.

On section (fig. 3) the tumor was seen as a ballooned-out, thin walled, osteomembranous sac filled with dark purplish red to maroon colored, cellular, friable tissue grossly resembling hyperplastic bone marrow. Of uniform consistency throughout, this tissue tended to separate either into firm, jelly-like chunks, or adhere to the tumor wall. No cysts or areas of degeneration were present.



Fig. 2 (case 2).—Right knee showing a neoplasm occupying the head of the fibula; the expanded, rarefied, well circumscribed area involving all the epiphysis of the fibula forms a picture characteristic of giant cell tumor.

The marrow cavity of the fibula extended up to the tumor where tumor substance and marrow merged into each other.

Histologic Examination.—Great numbers of giant cells of the epulis type or osteoclasts, varying much in size, and containing varying amounts of finely granular, acidophil cytoplasm, often vacuolated, and from ten to sixty small, ovoid, centrally placed nuclei with prominent nucleoli were seen more or less uniformly

embedded in a stroma composed of loose intercellular, fibrous reticulum (figs. 4 and 5). A few elongated, adult fibroblasts were seen here and there. Numerous rounded and polygon shaped cells, each containing a large vesicular nucleus and a considerable amount of rather deeply staining cytoplasm were scattered through the stroma. These had the general morphology and appearance of osteoblasts or liberated bone cells. At the periphery small plaques of bone surrounded by osteoblasts and a dense layer of fibrous tissue were seen. The stroma showed no evidence of unusual growth, and the general picture was characteristic of benign giant cell tumor.

CASE 3.—*History*.—N. P., an Irish girl, aged 25, entered the Radiological Clinic of the Philadelphia General Hospital, Aug. 12, 1925, complaining of pain and swelling in the right knee and inability to walk without crutches. In February, 1924, eighteen months previously, she had first noticed pain in the knee when

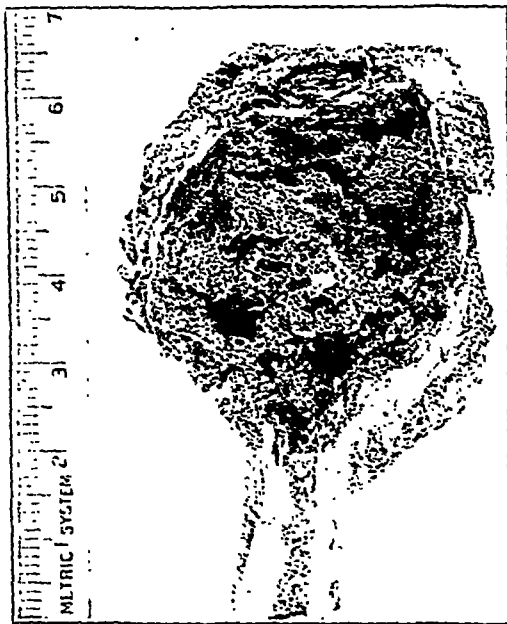


Fig. 3 (case 2).—Giant cell tumor of the head of the fibula treated by resection; ballooned-out osteoperiosteal sac filled with chunks of friable, cellular, bone free tumor substance; the limiting tumor wall is everywhere intact; a bony shell is seen circumscribing the growth in places.

standing, usually more pronounced in the morning. There was no history of injury. This condition had slowly grown worse and the knee had become somewhat swollen. For the four months preceding admission she had been unable to walk without crutches. It is interesting that because of a vaginal discharge, which proved to be of nonsyphilitic nature, the condition was thought to be a gonorrheal arthritis in three different hospitals, and was treated by baking, a roentgen-ray examination never having been made.

Physical examination revealed a swollen, stiff knee and slight pitting edema of the right leg and foot. The knee was slightly tender to pressure. The other physical findings were unimportant. The routine laboratory examinations were negative and the Wassermann reaction was negative. Roentgenologic study (fig. 6) showed a circumscribed rarefaction, diffusely mottled, occupying the greater

part of the epiphysis of the right femur, and practically all of the external condyle. A narrow bony rim bordered the scallops of this area on the internal side, but was lost on the extreme fibular side. Except for this irregularity, the area of bone tissue loss presented a multiple, coalescing, cystic appearance.

September 12, the leg was amputated at the level of the middle and lower third of the thigh. The wound healed by first intention, convalescence was

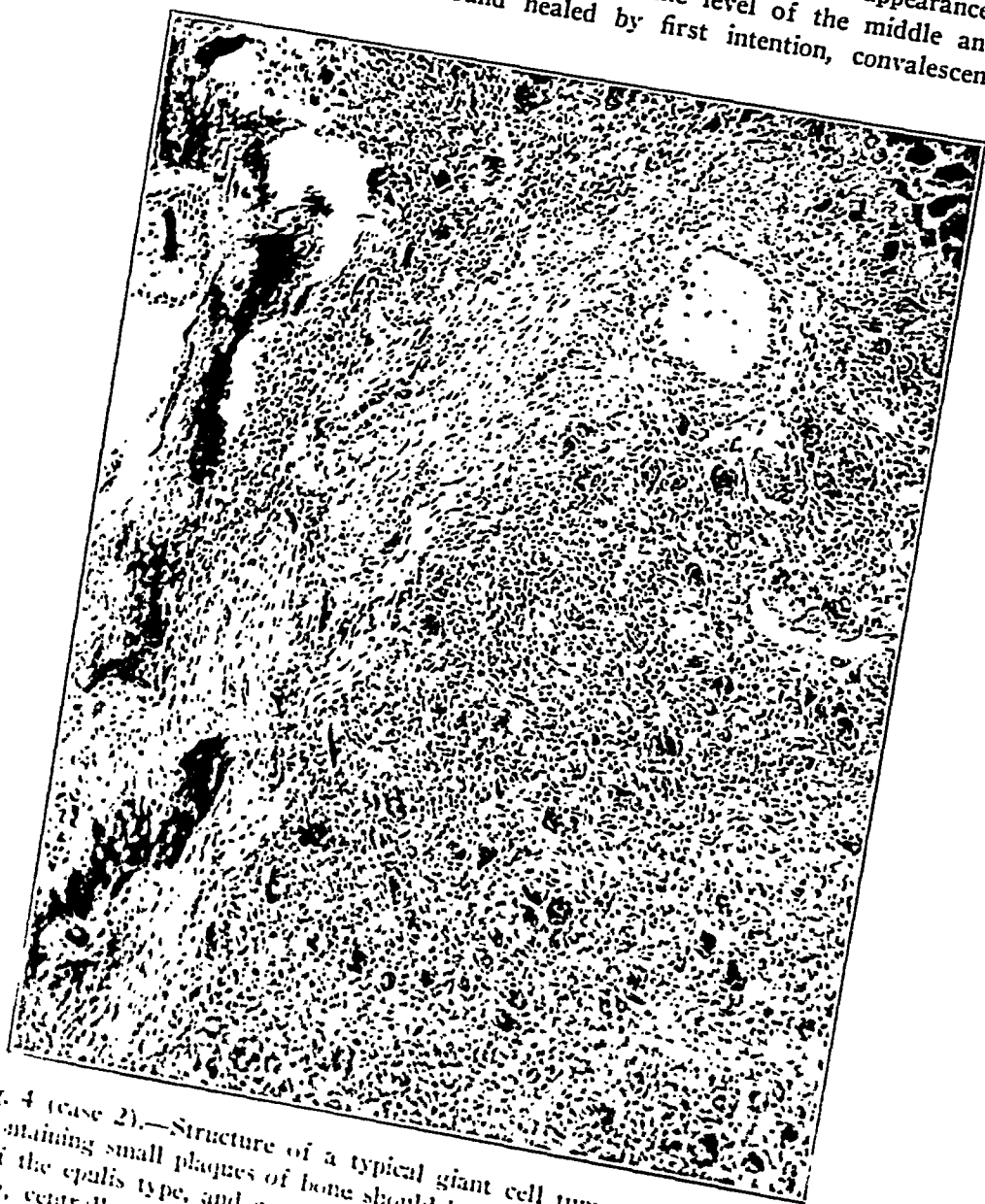


Fig. 4 (case 2).—Structure of a typical giant cell tumor: Limiting periosteal wall containing small plaques of bone should be noted. Many osteoclasts, or giant cells of the epulis type, and containing from fifteen to forty small, ovoid, deeply staining, centrally packed nuclei are scattered diffusely throughout the stroma; $\times 70$.

successful, and when seen in April, 1920, the patient was in excellent health and without recurrence.

Pathology of the Tumor.—Grossly, when the soft tissues were dissected away from the femur, an irregular enlargement of the epiphysis, especially laterally, was noted. On the fibular side, a rather dense but relatively soft mass was

palpable through the periosteum. Nowhere had the tumor perforated or broken through the periosteum. On section (fig. 7) a well differentiated mass, roughly the size of an orange, and surrounded by a narrow rim of bone everywhere except on the fibular side, occupied all of the external condyle and a large part of the epiphysis. Its center was golden yellow and cheeselike and appeared necrotic; an irregular peripheral zone, averaging from 1 to 2 cm. in thickness, was of mottled

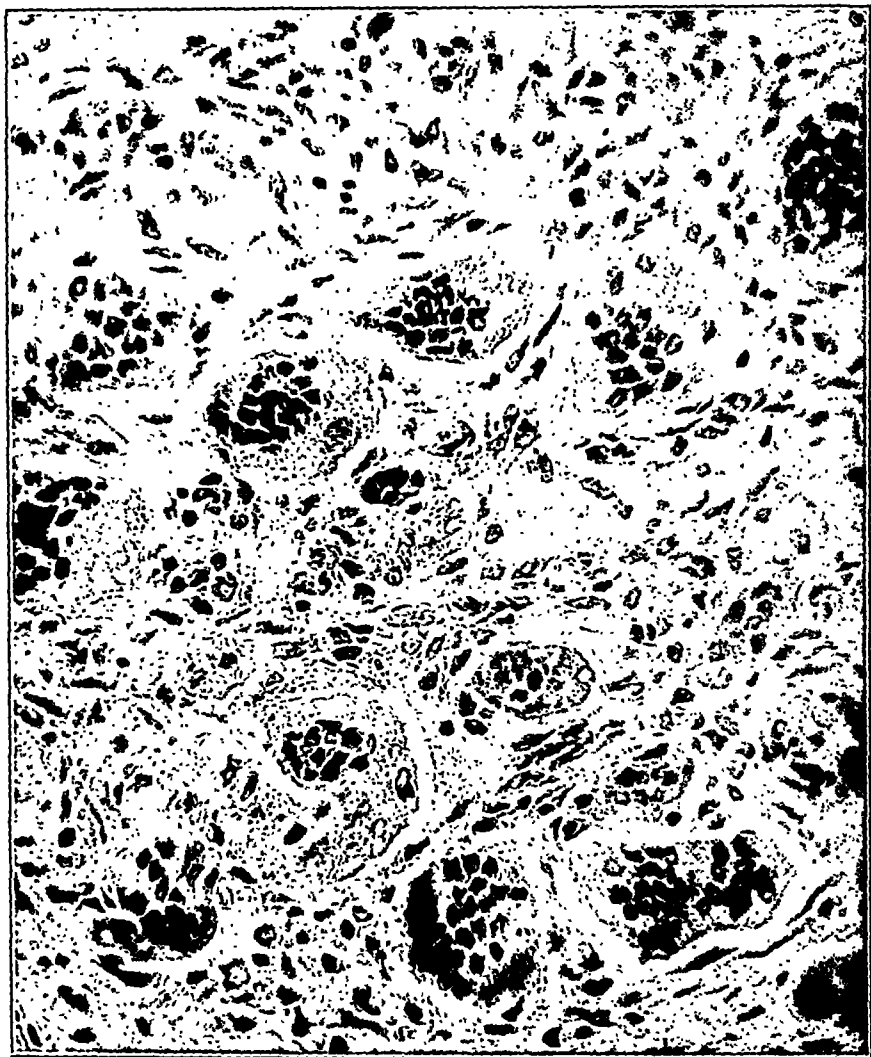


Fig. 5 (case 2).—Stroma composed of fine fibrous reticulum and numerous mature, elongated fibroblasts, under high power; in addition to the osteoclasts, many modified osteoblasts that have failed to eventuate into giant cells are seen embedded in the stroma.

gray red to deep wine color, and showed numerous small, rounded, firm, deep red, jelly-like patches. The tumor tissue was soft, friable and relatively bloodless, and no bony spicules were encountered.

Histologic Examination.—At the extreme periphery many small islands of bone tissue were seen (figs. 8 and 9). These were closely surrounded by a layer of cells, each containing one rounded, deeply staining nucleus, and a considerable

amount of granular, opaque cytoplasm. These had the general morphology of osteoblasts. Numerous large multinucleated giant cells of the epulis type were seen nearby, usually on the inner side of the bone plaques. These were interpreted as osteoclasts which were absorbing bone nearly as fast as it was formed. Many of these osteoclasts and numerous polygon shaped, mononuclear cells resembling osteoblasts or liberated bone cells were embedded diffusely throughout the tumor in a groundwork composed chiefly of loose fibrous reticulum and elongated, mature fibroblastic cells, which presented no signs of activity. A few



Fig. 6 (case 3).—Right knee, anteroposterior and lateral views, showing a neoplasm growing in the epiphysis of the femur; the rounded, mottled area of diminished density, bordered by a narrow, bony rim in places and with a scalloped periphery generally, forms a picture suggestive of multiple coalescing cysts but characteristic of giant cell tumor; only the periosteum limits the growth on the extreme fibular side.

poorly formed capillaries were noted. Sections from the central portion of the tumor showed that much of the growth had degenerated and had become necrotic. Microscopically this neoplasm presented no evidences of true malignancy, and was considered a benign giant cell tumor.

CASE 4.—*History*.—G. H., a white man, aged 32, entered the Polyclinic Hospital, March 11, 1923, in Dr. J. B. Carnett's service, complaining of pain in the right leg below the hip. Six months before he first noticed that when weight

was borne on the right leg there would be pain deep in the thigh, about 4 inches (10.1 cm.) below the hip. There was no history of injury. The condition had become only slightly worse, and two weeks before admission he had received an application of radium, which had practically relieved his pain. Physical examination was essentially negative, except for slight swelling of the greater trochanteric region on the right side. Motion of the thigh was not affected and there was no tenderness. The laboratory findings were negative. Roentgen-ray examination revealed rarefaction of the neck and trochanter of the femur, surrounded by a



Fig. 7 (case 3).—Femur showing a solid giant cell tumor occupying the greater part of the epiphysis; the irregular, dark patches at the periphery of the growth were maroon, jelly-like pockets in the fresh specimen; the center was yellowish and cheeselike; growth has not perforated the periosteum anywhere; the bony rim surrounding the tumor can be seen in places.

narrow rim of bone, everywhere intact (fig. 10). The contiguous bone appeared normal. The circumscribed area measured approximately 3 by 4 by 5 cm. A diagnosis of central sarcoma was made and, on March 23, the tumor was removed by Dr. Carnett by thorough curettement. Convalescence was uneventful. Roentgenograms made in November, 1923, eight months after operation, showed that recalcification to the extent of normal density had occurred. In April, 1926, the patient was well without signs of recurrence and was actively engaged in business as a traveling salesman.

Pathologic Examination.—The gross specimen consisted of several small chunks of reddish, firm, friable tissue, intermingled with considerable blood clot. No bone elements were demonstrable. Microscopic study of sections taken from different portions of the growth all gave the same picture (fig. 11). Large cellular patches composed of fine, loose, fibrous reticulum in which mature appearing fibroblasts grew in all directions formed a dense ground substance, throughout which many giant cells of the epulis type, or osteoclasts, were scattered. Imperfect capillaries were noted here and there and in places areas of hemorrhage were

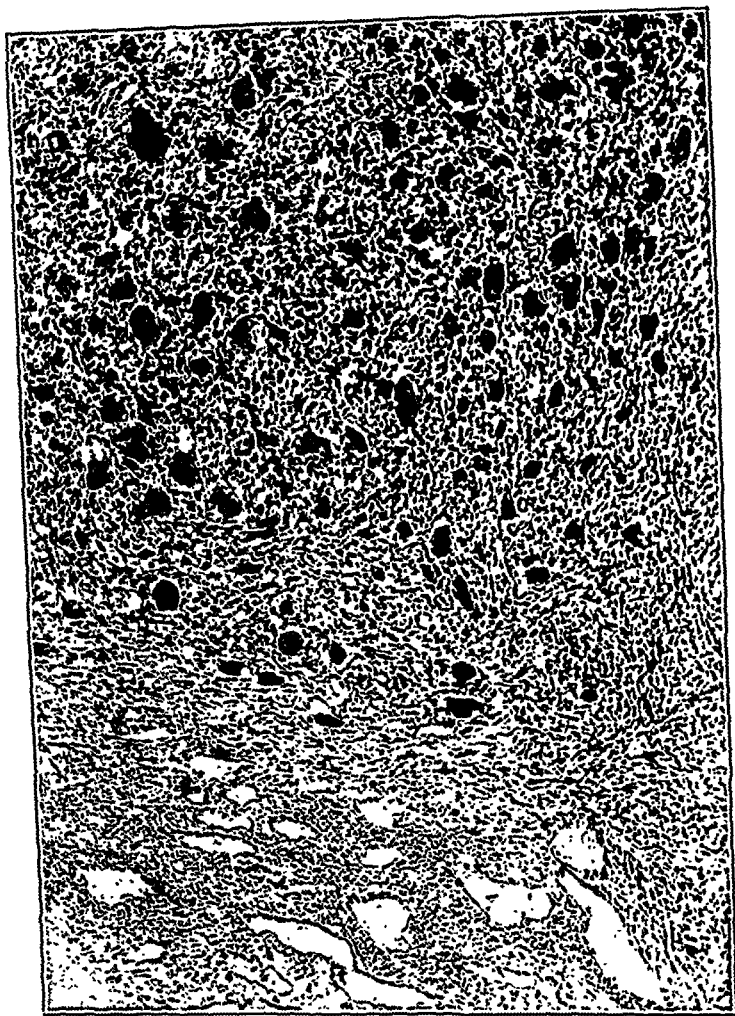


Fig. 8 (case 3).—More cellular giant cell tumor; many osteoclasts are scattered through the growth; the numerous osteoblasts, or liberated bone cells that have not taken part in giant cell formation, give the stroma an increased but pseudo-cellularity; $\times 115$.

prominent. This neoplasm, although possessing an unusually cellular stroma, showed no evidences of cell activity or malignancy, and because of the general adult appearance of its stroma, was regarded as a benign giant cell tumor.

These four cases are rather typical examples of the benign giant cell tumor, the most common of the central bone lesions. Occurring characteristically in the epiphyses of the long bones of young adults, with pain and swelling as initial symptoms, the disease progresses slowly and

in from three to eighteen months disturbance of function becomes the chief complaint. The roentgenograms in each instance show typically the circumscribed, diffusely mottled, rarefied area produced by the bone absorption activity of the everexpanding growth. Histologically, all four cases are benign. Osteoclasts, or giant cells of the epulis or foreign body type, are present in each in varying numbers and their significance, aside from the fact that they characterize the tumor by their presence, appears to be that of functioning mainly as bone absorbers. The stroma

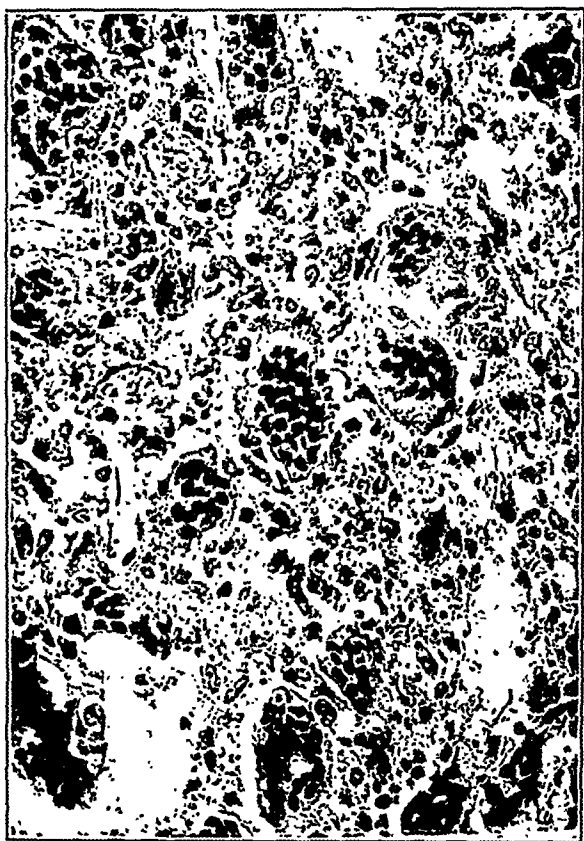


Fig. 9 (case 3).—Same section as shown in figure 8 under high power, showing the loose stroma, composed of a fine, fibrous reticulum and numerous adult elongated fibroblasts, which show no signs of activity; the polygon shaped mononuclear cells embedded in the stroma have the general morphology of osteoblasts and represent the liberated bone cells that have failed to fuse into polynucleated osteoclasts.

ranges from a relatively acellular fibrous matrix in case 1 to increasingly cellular structures composed chiefly of fibrous reticulum and fibroblastic cells in the other three cases, but in no instance do these cells show unusual behavior or activity. In each case the general adult appearance of the stroma is a fair criterion of the innocence of the tumor, and the follow-up shows that all four patients are well without signs of recur-

rence, four years, one month, seven months and three years after operation, respectively.

CASE 5.—(Drs. M. B. Cooperman and E. A. Case, Polyclinic Hospital).—*History.*—L. G., a white man, aged 34, stated that in 1916 he struck his left knee against a chair. Pain and slight swelling followed. Dry heat and hot baths were employed, but the condition failed to improve and in a few months he entered the Polyclinic Hospital, where a diagnosis of giant cell tumor was made. Thorough curettement of the tumor was done in 1917, one year after the initial injury.



Fig. 10 (case 4).—Pelvis showing a neoplasm occupying the neck and trochanter of the right femur; a narrow rim of bone surrounds the mottled area of diminished density and forms a picture typical of giant cell tumor. The growth was removed by thorough curettement and there has been no recurrence in three years.

The growth recurred after a period of apparent cure, and in 1919 a second curettement was done. Little benefit resulted from this; a second recurrence was soon evident, and on the third admission to the hospital the patient complained of inability to use the left leg and frequent attacks of sharp, needle-like pains throughout the knee. He had used braces and crutches the last ten months. Physical examination revealed an irregularly enlarged knee, twice normal in size, with complete loss of function. It was tense and tender and quite hard, but softer in spots than in others. Other physical findings were of no consequence,

and the routine laboratory examinations were negative. The Wassermann reaction was negative. A roentgenogram (fig. 12) showed a bone destroying neoplasm involving the upper part and head of the left tibia, the head of the fibula, and the posterior portion of the internal condyle of the femur. The leg was amputated well above the knee in October, 1921.

In August, 1922, the patient again returned to the hospital, complaining of cough, substernal pain on coughing, and of blood spitting of five months' duration. He had lost much weight and had grown progressively weaker. Roentgen-ray exam-



Fig. 11 (case 4).—Giant cell tumor with a cellular stroma; many mature, elongated fibroblasts growing in every direction form this stroma; no mitoses are seen; the osteoclasts are present in large numbers and are uniformly embedded throughout the growth; $\times 275$.

ination of the chest (fig. 13) revealed metastatic lesions in the lungs. The patient failed rapidly and died in November, 1922. Necropsy was not performed.

Pathologic Examination.—Tissues from the first and second curettements unfortunately were not available for this study, but were reported as showing the structure of typical giant cell tumor. Dissection of the tumor in the amputated leg (fig. 14) revealed a destructive, soft, cellular, invasive, sarcomatous growth involving all the bones and soft tissue about the knee joint.

Sections taken from different portions of the neoplasm (figs. 15, 16 and 17) showed many areas composed of closely packed, thick, spindle shaped cells, scattered through which were numerous large, multinucleated giant cells of the epulis

type. Very little fibrous supporting tissue was present. Other areas consisted almost exclusively of spindle cells, relatively constant in size and staining reaction but showing numerous karyokinetic figures, suggesting rapid growth. Still other areas consisted of closely packed, varying sized, deeply staining, rounded or polyhedral cells, scattered through which were many irregular giant cells, not of the

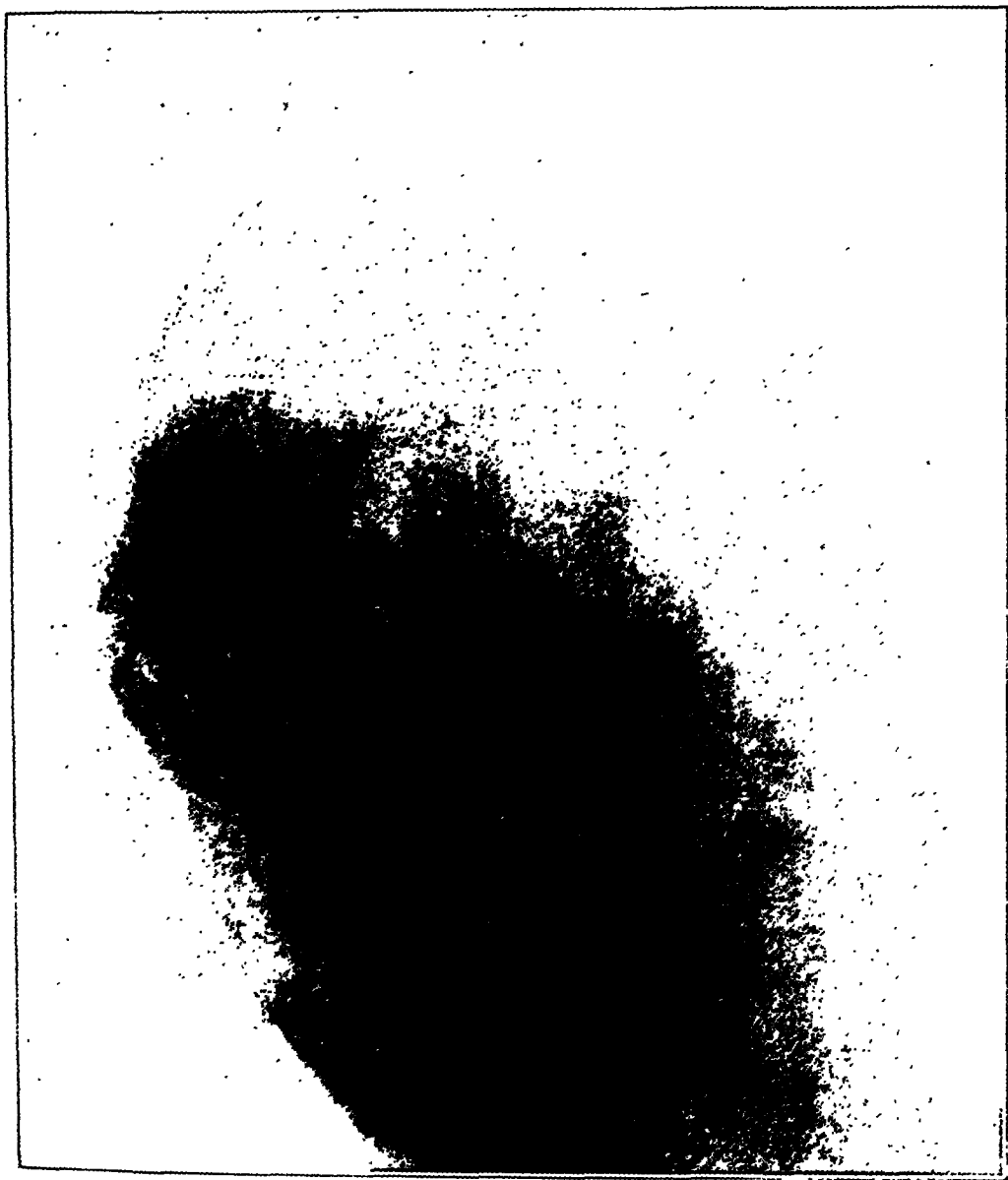


Fig. 12 (case 5).—Left knee region showing the second recurrent neoplasm of the head of the tibia five years after the initial growth and following two curettements; there is massive involvement of the entire knee with destruction of the head of the tibia, fibula and lower part of the femur and obliteration of the knee joint. This neoplasm is basically a giant cell tumor but has undergone malignant transformation.

epulis type, containing varying amounts of cytoplasm and from one to four or five large, deeply staining oval nuclei, many of which were dividing. No areas of calcification or ossification were demonstrable. Dr. E. A. Case of the Polyclinic



Fig. 13 (case 5).—Chest showing metastatic tumor shadows in the right lower lobe, in the left upper lobe and substernally.

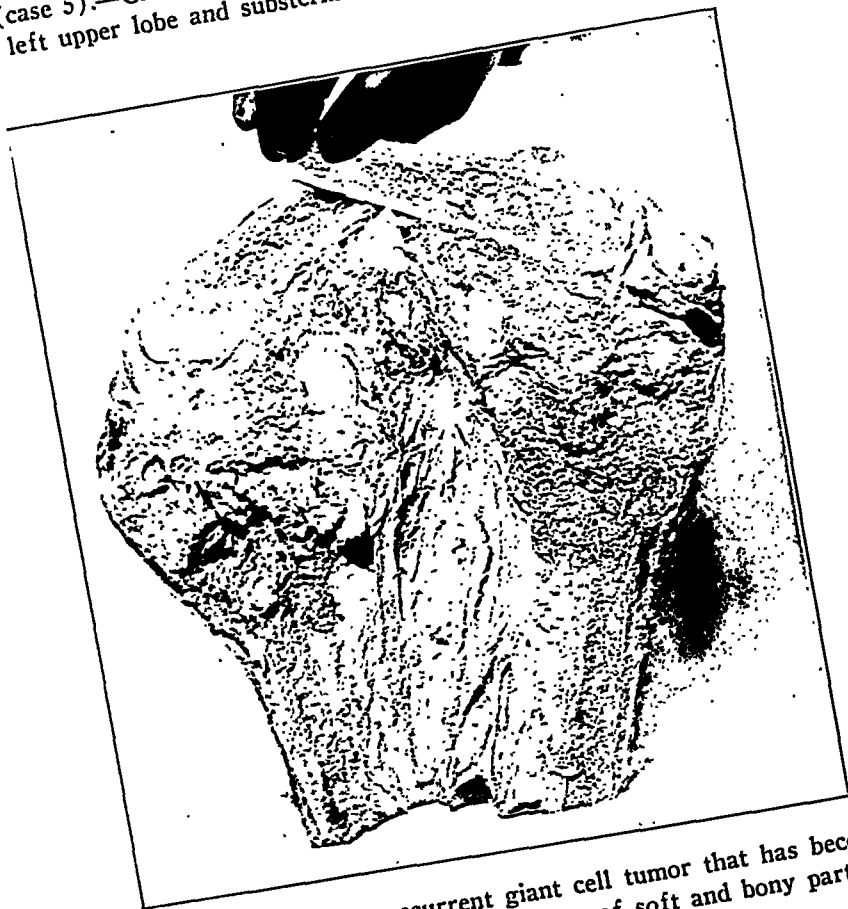


Fig. 14 (case 5).—Massive recurrent giant cell tumor that has become malignant, showing extensive invasion and destruction of soft and bony parts about the knee.

Hospital described the condition as "giant cell sarcoma with a number of areas of actively growing cells," and our study of the various sections suggested that basically the tumor was a true giant cell tumor, which now showed malignant transformation, an opinion in which Dr. James Ewing concurred.

This case is both atypical and unusual. The history, symptoms, behavior and clinical study of the tumor in its early course all point rather strongly to its "benign giant cell tumor" nature originally and, although the tissues and slides from the first and second curettements unfortunately were not available for our study, histologic confirmation may perhaps be assumed on the grounds that the pathologic diagnosis at

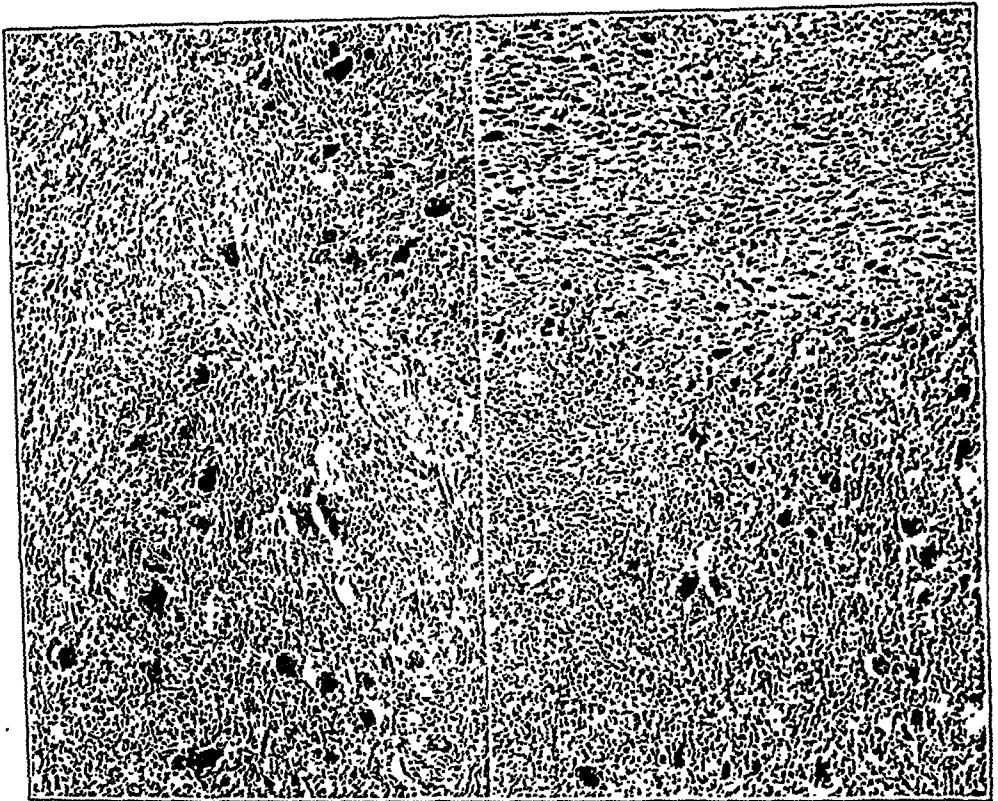


Fig. 15 (case 5).—Structure of a giant cell tumor that has undergone malignant transformation, under low power; the stroma is extremely cellular, composed chiefly of spindle cells and is without giant cells in places; the large giant cells are of the epulis type and were present throughout the growth in patches; the smaller, deeply staining giant cells are of the malignant type.

the time of each operation was "giant cell sarcoma." Microscopic study of tissues obtained at the time of amputation confirms definitely the malignant nature of the growth at this time, yet but for the numerous areas of actively growing, atypical cells, the picture remains basically that of giant cell tumor with a cellular stroma composed chiefly of active, fat spindle cells. The tumor followed injury; was treated by curettement after a year; recurred and was treated again by curettement two years later; recurred a second time with the aspects of malignancy and was

treated by amputation five years after and caused death by metastasis, proved roentgenologically, six and one-half years after the appearance of the original growth; so it would seem that we are dealing with a true giant cell tumor that had undergone malignant transformation. A parallel to this case is one reported by E. F. Finch and H. H. Gleave,¹⁶ microscopic sections from which we have had the privilege of studying, and the salient features of which are as follows:

A man, aged 49, entered the Sheffield Royal Infirmary in December, 1917, with a pathologic fracture of the lower end of the femur, which apparently healed satisfactorily without surgical treatment, and a history of pain in the knee since 1915. A roentgenogram made at this time revealed the presence of a tumor

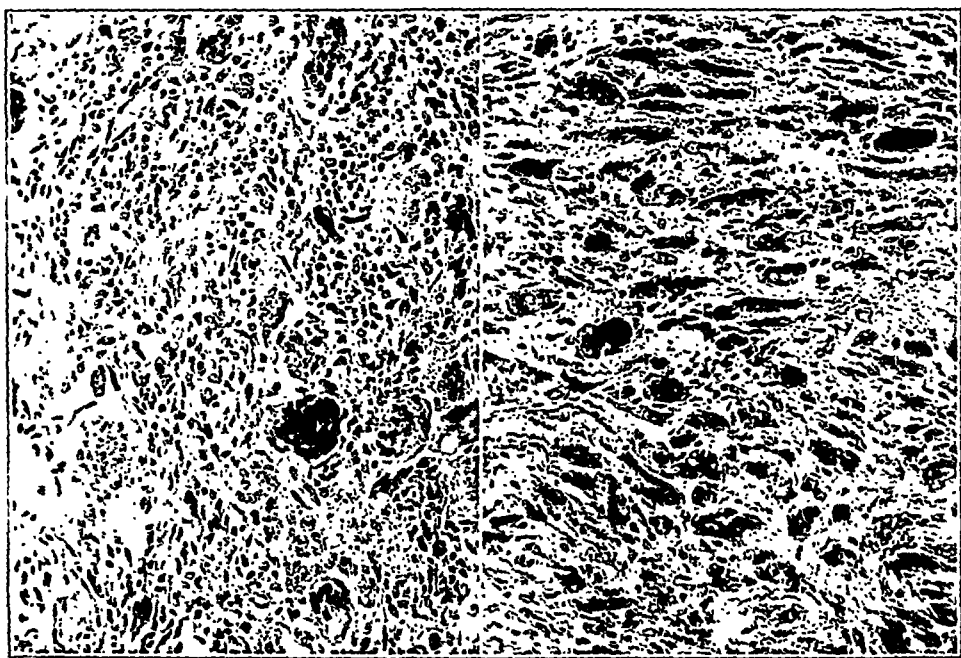


Fig. 16 (case 5).—Recurrent malignant giant cell tumor showing in detail to the left an area fairly typical of giant cell tumor, under high power; the stroma is very cellular and is composed of spindle cells, some of which show mitotic figures; the giant cells are of the epulis type and show no changes; to the right is an area composed of large, plump, spindle cells and giant cells of the malignant type containing large, hyperchromatic nuclei.

at the site of the fracture, and in June, 1920, when there was pain and swelling at the same site, roentgen-ray examination gave a typical picture of central giant cell tumor. The patient refused operative treatment and, fitted with a splint, continued at work as a carpenter until September, 1924, when the pain became quite severe. The leg was amputated in January, 1925, and gross study and dissection showed a typical appearing currant jelly tumor, which had extended

16. Finch, E. F., and Gleave, H. H.: A Case of Osteoclastoma (Myeloid Sarcoma, Benign Giant Cell Tumor) with Pulmonary Metastasis, *J. Path. & Bact.*, to be published.

through the line of fracture into the thigh muscles and which had partially obliterated, but not invaded, the knee joint. Sections from this growth gave a typical giant cell tumor picture with a groundwork of pleomorphic and fibroblastic cells, which contained many osteoclasts, or multinucleated giant cells of the epulis type. In October, 1925, there was a recurrence of the growth in the stump, and a history of hemoptysis of three months' duration. Roentgen-ray examination revealed pulmonary metastasis. The patient died in January, 1926. At necropsy a massive, locally malignant, recurrent tumor, 8 inches (20.3 cm.) in diameter, and involving the whole of the stump, and numerous soft, whitish and hemorrhagic secondary tumor nodules in the lungs were demonstrated. Microscopic study of sections from the stump recurrence gave essentially the same picture as was noted at the time of amputation, except that the stroma was more cellular and showed many mitotic figures. The osteoclasts showed no changes. Sections from the lung

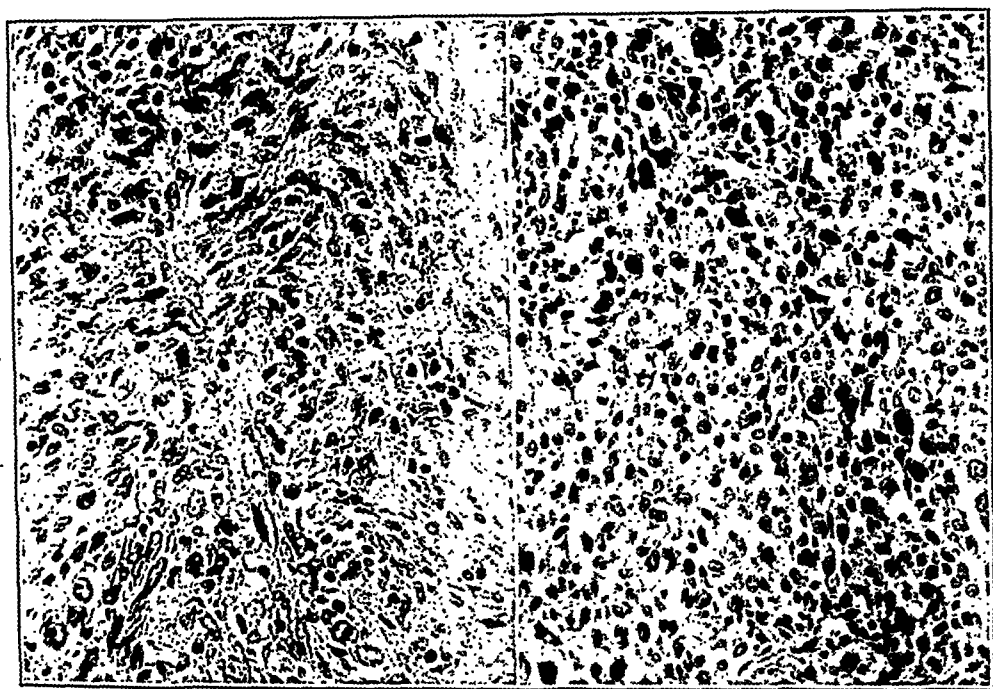


Fig. 17 (case 5).—Same neoplasm as shown in figure 16, under high power, showing to the left a patch of large, rapidly growing, closely packed spindle cells; no giant cells are seen; to the right is an area composed of pleomorphic cells, many showing cell division stages; the picture resembles that of mixed cell sarcoma.

metastases were practically identical with these. The stroma was composed of fibroblastic, actively growing cells, and scattered uniformly throughout many multinucleated osteoclasts were demonstrable.

CASE 6 (Drs. E. B. Hodge and J. Eiman, Presbyterian Hospital).—*History*.—S. C., a white man, aged about 22, entered the Presbyterian Hospital in January, 1923, complaining of pain, swelling and tenderness in the left knee. Two months prior to admission he had first noticed soreness and stiffness in the knee joint. There was no history of injury. The condition had grown steadily worse and on admission the joint was practically functionless. Physical examination revealed fluid in the knee joint and fullness about the lower end of the femur. Roentgenologic study (fig. 18) revealed an indefinitely circumscribed area of haziness about 5 cm. in diameter, occupying the posterior portion of the lower end of the left femur

and apparently extending through the periosteum. Bone formation was not evident. Giant cell tumor was suspected, and, at operation, a pocket containing a "quantity of reddish fatty material suggestive of blood clot" was found, and treated by thorough curettement. Convalescence was uneventful, but the tumor recurred locally in a short time and in six months the patient died with clinical signs of widespread metastasis.

Pathologic Examination.—Histologically, sections taken from different portions of the tumor (figs. 19 and 20) showed a loose, spongy stroma composed of

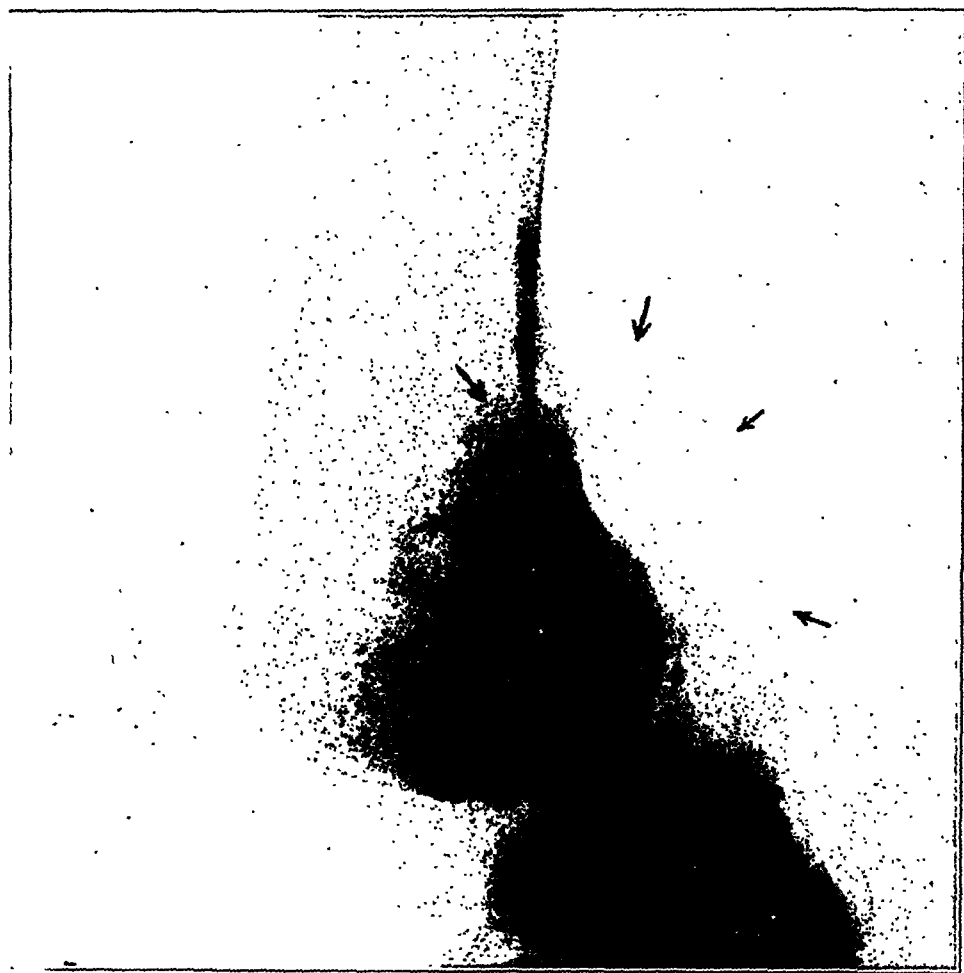


Fig. 18 (case 6).—Lateral view of left knee showing a lesion, indicated by the arrows, in the lower posterior portion of the femur; the ill-defined, noncircumscribed area of slightly increased density apparently extending through the periosteum posteriorly is not the picture of giant cell tumor; histologically, this case proved to be an osteogenic sarcoma which secondarily contained giant cells of the epulis type.

irregular sized and shaped cells, many of which were undergoing cell division. Some of these cells approached giant cell size but contained only one large, hyperchromatic nucleus. No supporting reticulum was present. Scattered diffusely throughout the growth were seen giant cells of the epulis type, containing from ten to forty small, oval, centrally placed nuclei. Here and there small foci

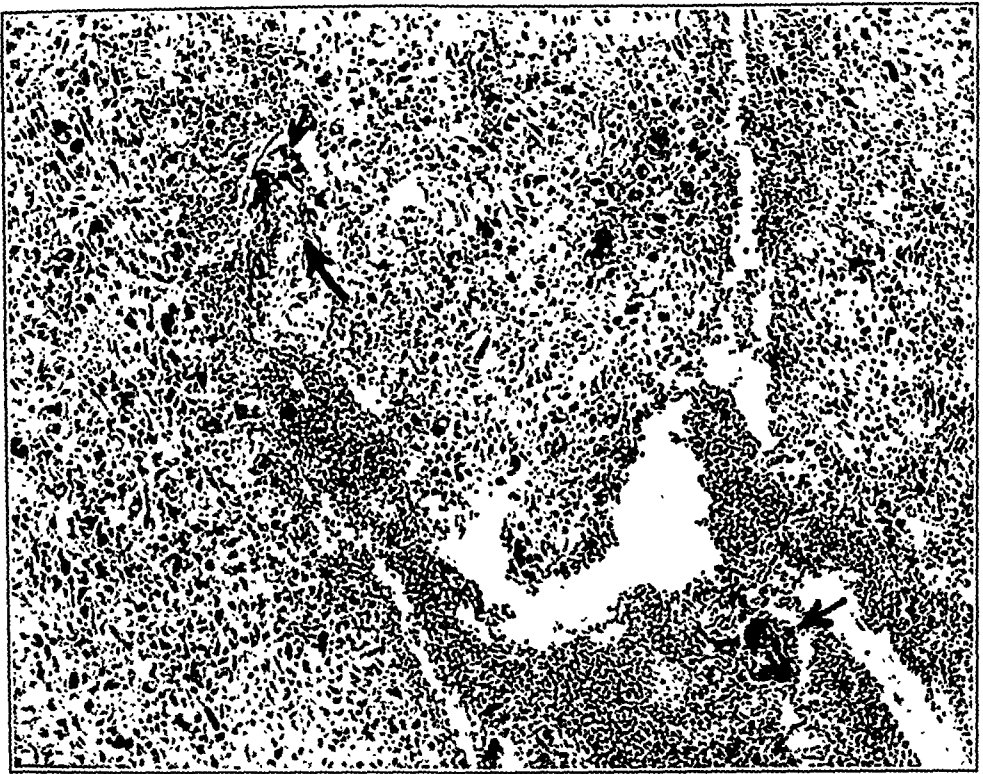


Fig. 19 (case 6).—Osteogenic sarcoma secondarily containing giant cells of the epulis type; two foci of bone formation may be seen near the area of hemorrhage; numerous osteoclasts are recognized in the cellular stroma; $\times 115$.

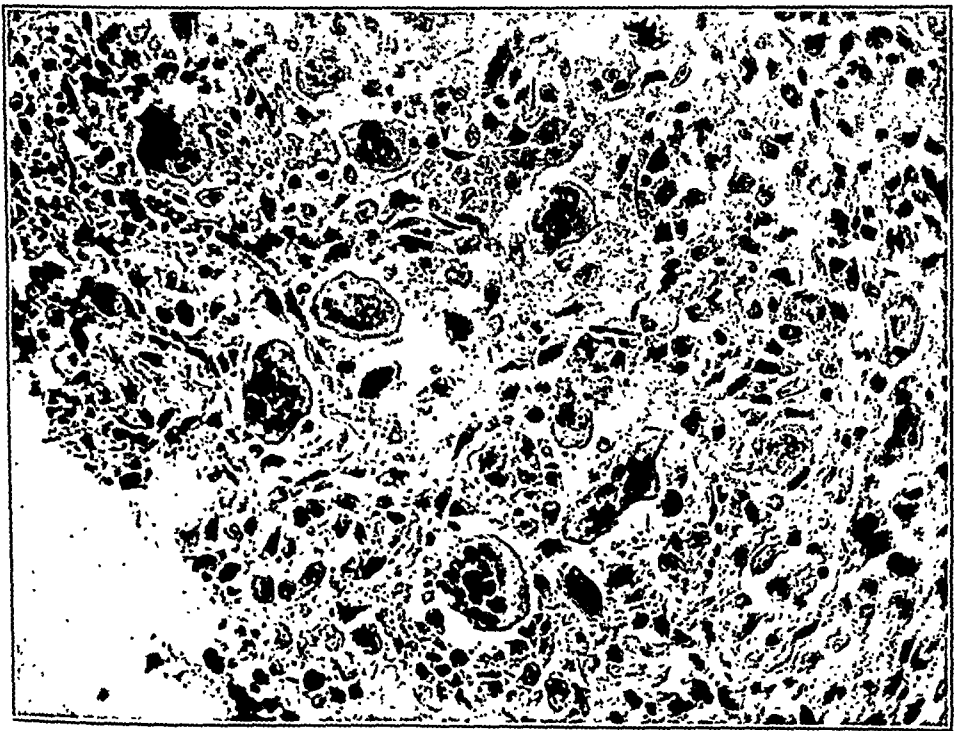


Fig. 20 (case 6).—Same sarcoma as shown in figure 19 showing numerous giant cells of the epulis type scattered throughout the stroma, which is composed of actively growing pleomorphic cells; the osteoclasts obscure the picture until the stroma is analyzed; $\times 275$.

of calcification and ossification were demonstrable. Microscopically the picture was that of an osteogenic sarcoma containing giant cells of the epulis type, rather than a giant cell tumor that had undergone malignant change. Dr. James Ewing concurred in this diagnosis.

This case is confusing. Occurring in a young adult in a site frequently elected by giant cell tumors, this neoplasm gives the rather striking history that it has from the outset grown quite rapidly. The roentgenogram is both indefinite and atypical, and although the gross appearance of the lesion suggested that it might be of innocent nature, histologic study shows clearly that the tumor is basically malignant. The occurrence of numerous innocent appearing, multinucleated giant cells of the epulis type throughout the growth further obscures a picture that is already generally atypical and is significant in indicating the bone absorption activity of the neoplasm. Proper evaluation of the nature of the growth, however, is arrived at by a critical analysis of the stroma, and evidences of malignancy are recognized in its abundance of actively growing cells and in the many tiny centers of bone formation scattered throughout. Confirmation of this diagnosis is proved by a fatal outcome shortly after operation.

COMMENT

These cases are sufficiently varied that certain helpful points can be gleaned from their study, even though generalizations are not warranted. They illustrate well some of the difficulties that are likely to be encountered in dealing with central bone tumors in arriving at a correct diagnosis on which proper treatment and prognosis depend. A carefully taken history, thorough clinical study and critical roentgen-ray examination in the majority of instances establish fairly definitely and accurately the general nature of the growth, but microscopic analysis, we feel, offers the surest criterion of the specific nature and relative malignancy of the tumor. It is hardly necessary to add that a rigid and frequent "follow-up" of any bone lesion is imperative, if we are to be finally checked on our impressions regarding bone tumor behavior.

The histologic structure of the giant cell tumors gives one a rather definite criterion of the neoplasm's relative aggressiveness. An analysis of the stroma, with particular attention to its cellularity, cell type and cell activity, permits one to estimate fairly accurately the degree of malignancy any given tumor may possess. The more cellular stromas, composed of fibroblastic or spindle cells, and showing cell division stages, can be said to grow considerably more rapidly than the relatively acellular adult fibrous ones lower down the scale. In this connection, it is interesting to note that recurrent growths practically always present a noticeably more malignant appearing stroma microscopically than the primary growth exhibited, the increase in stroma cellularity and activity being a fair measure of the recurrent tumor's increase in virulence.

The giant cells of the epulis type that are characteristically present vary considerably in number in different tumors and, as a rule, are relatively less abundant in tumors possessing the more cellular stromas. Their main function, apparently, is that of bone absorption, for which reason they may be properly designated *osteoclasts*, a term introduced by Kölliker.¹⁷

Our interpretation of the histogenesis of the giant cell tumor is that two mesoblastic tissues, the osteoblastic, or osseous tissue proper, and the fibroblastic, or specialized fibrous tissue framework, intimately associated in bone structure, as pointed out by Stewart,¹⁸ are the elements composing giant cell tumor. Study of the osteoclasts in their various stages of formation, best observed at the margin of the expanding tumor, suggests that they are derived from the osteoblastic element. Formed by the fusion of modified osteoblasts, or liberated and hypertrophied bone cells, as advocated by Kölliker¹⁷ and Gross,⁶ and possessing the faculty for further hypertrophy and multiplication, their variation in size, number and distribution in different tumors can be accounted for. Many of these modified osteoblasts, or liberated bone cells, fail to eventuate into giant cell formation and are recognized as the rounded and polygon shaped cells (figs. 5 and 9) embedded in the stroma along with the osteoclasts, this often giving an increased but pseudocellularity (fig. 8) to the stroma, which is likely to be misinterpreted. The osteoclasts, by virtue of their function and origin, have direct connection with tumor occurrence and in a sense may be regarded as specific neoplastic giant cells, but we consider them as being essentially innocent.

To the fibrous supporting reticulum and fibroblastic cells that constitute the stroma of giant cell tumor, we would ascribe origin from the specialized fibroblastic tissue, and we feel that the behavior of this structure governs the course of the growth. Such a conception would explain the innocence of a tumor with adult stroma at the lower end of the scale and the relative malignancy of the more cellular and immature stromas higher up, and is in keeping with the spindle cell or fibrosarcomatous picture that the majority of malignant growths have presented. In the rare instances in which osteoclasts were demonstrable in pulmonary metastases, their occurrence might be accounted for on the assumption that they were transported there by the metastasizing fibroblastic tissue.

A study of the behavior and course of the giant cell tumors emphasizes the fact that this bone lesion, whatever its true nature, possesses

17. Kölliker, A.: *Handbuch der Gewebelehre des Menschen*, ed. 6, Leipzig 1: 347-350, 1889.

18. Stewart, M. J.: *The Histogenesis of Myeloid Sarcoma*, *Lancet* 2:1106, 1922.

certain attributes that are recognized as features of tumor growth. Varyingly aggressive, it frequently exhibits its power of recurring locally after operative treatment and occasionally, particularly following pathologic fracture, its faculty for progressive, unlimited growth to the extent of invasion and destruction of nearby tissues is evident. In addition to this, it seems inescapable that this tumor may rarely actually metastasize, proof of which is offered in the cases cited in this study, and in references to other authentic cases. A lesion possessing such faculties should be regarded, it would seem, as a true neoplasm rather than a chronic inflammatory process and, although usually benign, as being always locally aggressive and in a sense potentially generally malignant. This conception establishes the guiding principle that giant cell tumors should be thoroughly eradicated as early as possible and at the first treatment, lest inadequate or improper treatment, whatever the choice, result in a local recurrence or perhaps in a malignant transformation of the growth.

SUMMARY

1. The known behavior of the giant cell tumor warrants its being classified as a true neoplasm.

2. The giant cell tumors constitute a series. Those at the lower end of the scale possess relatively adult fibrous stromas and are essentially benign. They exhibit more cellular and active stromas, composed chiefly of relatively immature fibroblastic cells and become increasingly more locally aggressive as the scale is ascended.

3. Under the stimulus of inadequate or improper treatment, they may recur locally, those at the upper end of the scale being especially liable to this tendency. Such recurrences, as a rule, are more aggressive or virulent than the primary growth, both clinically and microscopically.

4. They are potentially malignant and may as a result of repeated or improper treatment excitation on rare occasions undergo malignant transformation and metastasize.

5. The giant cells, or osteoclasts, that are characteristically present function as bone absorbers, and are of osteoblastic origin. They are not reliable indexes of the neoplasm's relative malignancy.

6. The stroma is of fibroblastic origin and its behavior governs the course of the giant cell tumor. Thorough microscopic study of its cellularity, cell type and cell activity offers a fairly reliable criterion of the innocence or relative malignancy of the growth.

7. History, thorough clinical and roentgen-ray study, macroscopic and critical microscopic analysis, and a rigid follow-up are all necessary in establishing the final correct diagnosis and the true nature and behavior of the giant cell tumor.

THE REGENERATION OF THE LYMPHATICS *

FREDERICK LEET REICHERT, M.D.

BALTIMORE

That lymphatics exist in new growths and newly formed tissues has been shown by injection experiments. That they regenerate in normal tissues was mentioned by the late Professor Halsted¹ in 1922 in his article concerning the replantation of limbs in animals. His statement was based on the experiments included in this article.

Probably the earliest observation on the regeneration of the lymphatics was made by Krause² in 1863. By making colored injections in the skin adjacent to tumors he demonstrated the continuation of true lymphatics into the tumors.

In his lectures on surgical pathology and therapeutics, Billroth³ in 1863 demonstrated specimens in which the lymphatics did not grow across scar tissue, at least not in early stages. After a 7 day old wound in the lip of a dog had healed by first intention the lymphatic vessels were injected. He said,

You see that the young cicatrix, on the seventh day, when it still consists almost exclusively of cells, has no lymphatic vessels; these cease immediately at the young cicatrix; they do not form in the cicatrix until the fibrillary connective tissue bundles form. The granulation tissue also has no lymphatic vessels; where the inflammatory new formation, where the primary cellular tissue forms, the lymph vessels are mostly closed, partly by fibrous coagulations, partly by new cell formations. These observations have also been confirmed quite recently by Löscher of St. Petersburg, by examination of traumatically inflamed testicles.

In Bartel's⁴ treatise on the lymphatic system in Bardeleben's Handbuch, he states that "Talke found in pleuritic membranes, newly formed lymphatics and capillaries as well as large lymphatics and lymphatic plexuses; besides, he saw lymph spaces." He also states that Poirier and Moran were able to inject abundant networks of lymphatics in recto-uterine adhesions.

* From the Department of Surgery, Johns Hopkins University Medical Department.

1. Halsted, W. S.: Replantation of Entire Limbs Without Suture of Vessels, Proc. Nat. Acad. Sc. 8:185, 1922.

2. Krause, W.: Ueber Lymphgefasse im geschwulsten, Deutsch. Klinik. 15: 377-378, 1863.

3. Billroth, T.: Die allgemeine chirurgische pathologie und therapie, Berlin, 1863, p. 90, figure 11.

4. Bartels, Paul: Das lymphgefasse system, Jena, 1909, no. 17, Handbuch de anatomie des Menschen, herausgeg, von Karl V. Bardeleben.

Bayer⁵ attempted to show by experiments on dogs that lymph glands recurred after their extirpation. By injecting limb lymphatics with india ink the axillary lymph nodes were demonstrated and were then excised. After stated intervals the limb lymphatics were again injected with cinnabar, and then the entire axillary contents removed and sectioned. In one animal no lymph nodules were found. In another a small, soft pea-sized gland containing cinnabar was the only evidence of lymph nodes. As some of the axillary fat was stained red he concluded that lymph glands recur from the surrounding fat. On the basis of these experiments, together with certain pathologic material, he developed the theory that lymphatic glands were formed from fat and that fat was part of the lymphatic system.

About the same period Delius⁶ conducted the experiments which led him to believe that regeneration took place when portions of a gland were excised. Ribbert⁷ also believed that regeneration followed excision of portions of the submaxillary lymph gland.

Heuter⁸ and later Meyer⁹ were unable to find any experimental evidence of regeneration in glands and the latter found no recurrence following the extirpation of the popliteal glands. Meyer suggested that following the resection of mesenteric glands, the reestablishment of lymphatic connections with the receptaculum chyli was probable but not proved. He therefore attempted to test the question of regeneration of lymphatic vessels by ligating and dividing the main lymphatic trunks lying on either side of the saphenous vein, near the knee of the dog. In eight cases studied, fourteen to ninety-one days after operation, injections showed no regeneration of these vessels. He concluded that if stasis were the main stimulus to regeneration it was quite probable that resection and ligation of one or two principal trunks in the region of the knee and elbow did not interpose sufficient obstruction to the flow of lymph.

Coffin¹⁰ brought a loop of intestine outside the abdominal wall. Ten days later the lymphatics of the loop were injected and new lymph

5. Bayer, Karl: Ueber regeneration und neubildung der lymphdrusen, *Ztschr. f. Heilk.* 6:105, 1885.

6. Delius: Ueber die regeneration der lymphdrusen, dissertation, Bonn, 1888, quoted by Meyer, A. W.: *An Experimental Study on the Recurrence of Lymphatic Glands and the Regeneration of Lymphatic Vessels in the Dog*, *Bull. Johns Hopkins Hosp.* 17:185, 906.

7. Ribbert: *Beitr. z. path. anat. u. allg. path.* 6, 1889, quoted by Meyer (footnote 6).

8. Heuter: *Verhandl. d. deutsch. path. Gesellsch. f. Chir.*, 1904, quoted by Meyer (footnote 6).

9. Meyer (footnote 6).

10. Coffin, T. H.: *On the Growth of Lymphatics in Granulation Tissue*, *Bull. Johns Hopkins Hosp.* 17:277, 1906.

vessels could be seen in the granulation tissue surrounding the intestinal loop. Thus it seemed conclusive that lymphatic channels had grown into the overlying granulation area from the lymphatics of the intestinal wall.

Evans¹¹ in 1908 reported the growth of lymphatics into malignant tissue, a metastatic sarcomatous nodule in the intestinal wall. He injected the intestinal lymphatics and found the delicate lymph channels of the nodule in direct connection with the preexisting and neighboring lymphatic plexus. The newly formed lymphatics seemed to be capillaries and to have arisen from the mucosal system.

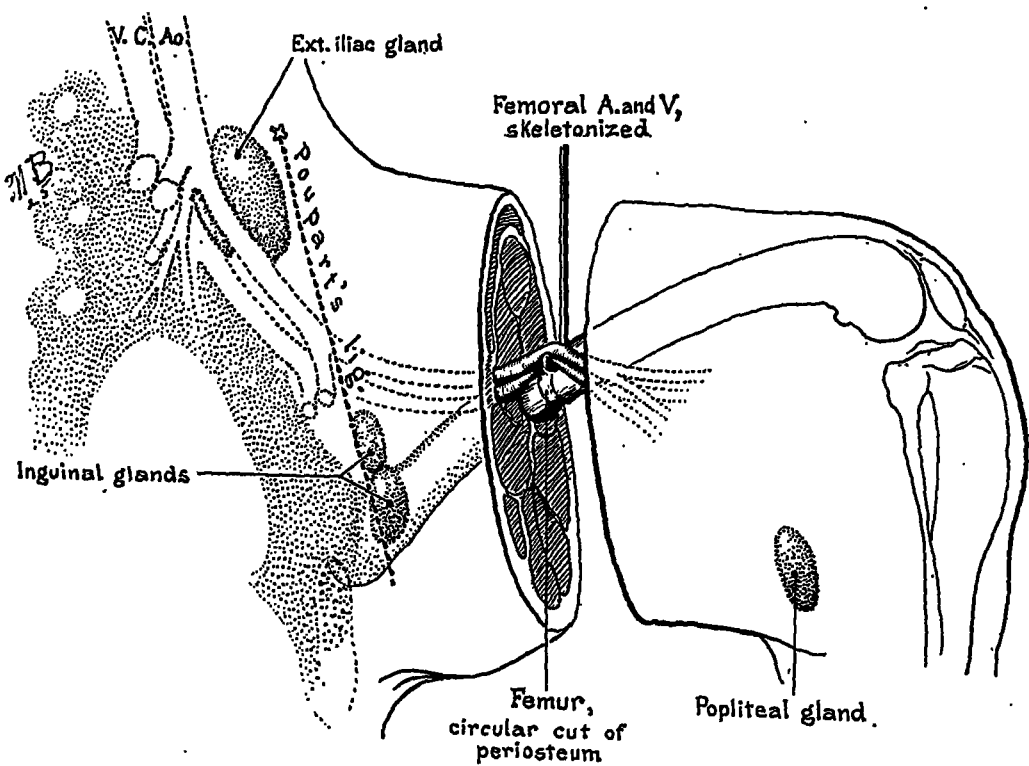


Fig. 1.—Division and isolation of structures in the replantation of a dog's thigh.

When inquiring into the cause of edema of transplants of skin and soft parts Eloesser¹² expressed the view that scar tissue caused edema by blocking the lymphatics. He made incisions across the dorsum of a rabbit's ear. The wound, which extended down to the broad cartilage, was allowed to heal by granulation. Although barium sulphate injections did not pass beyond the scar, small lymphatics could be traced across

11. Evans, H. M.: On the Occurrence of Newly Formed Lymphatic Vessels in Malignant Growths, *Bull. Johns Hopkins Hosp.* 19:232, 1908.

12. Eloesser, Leo: Obstruction to the Lymph Channels by Scar, *J. A. M. A.* 81:1867 (Dec. 1) 1923.

the wound in some instances when injections were made with india ink. This obstruction by scar tissue persisted as long as four months.

OPERATIVE PROCEDURE

Our experiments on the regeneration of lymphatics developed incidentally during attempts to produce experimental elephantiasis chirurgica in dogs.¹³ One of the procedures suggested by the late Professor Halsted for this study was replantation of a dog's hind limb. It was then possible to determine the degree of swelling which resulted from the

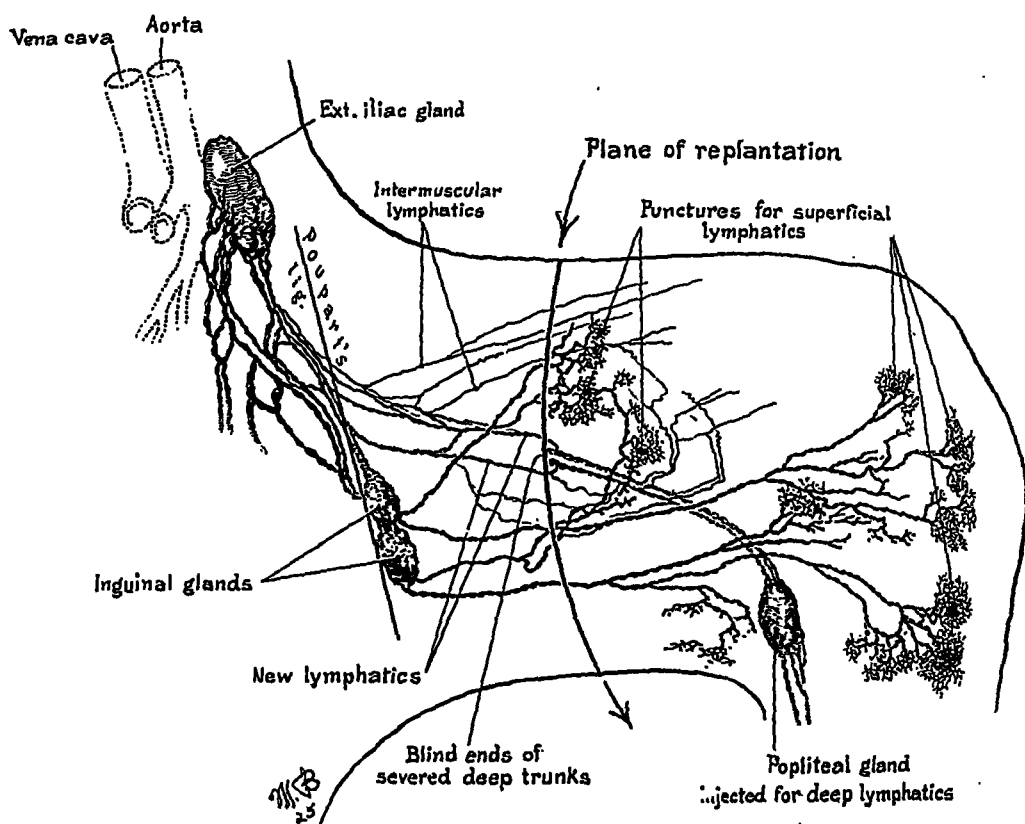


Fig. 2.—Regeneration of both the superficial and deep lymphatic sets after replantation of a dog's thigh (drawing of figure 3).

division of vessels and lymphatics. By a complete circular incision through the middle third of the thigh, the skin, subcutaneous tissue and muscle were divided transversely (fig. 1); only the femur, the femoral artery and vein were left intact and these remaining structures were carefully isolated and stripped of all areolar tissue. A circular cut was made through the periosteum and the outer part of the adventitial coat of the femoral vessels. This insured complete severance of all

13. Halsted, W. S.: The Swelling of the Arm After Operations for Cancer of the Breast—Elephantiasis Chirurgica—Its Cause and Prevention, *Bull. Johns Hopkins Hosp.* 32:309-314 (Oct.) 1921.

lymphatic vessels. The extremity, which had thus been practically amputated, was replanted by careful approximation of the muscle stumps and skin edges with silk sutures. These replanted limbs united without infection and with the least possible scar tissue, as shown by histologic study. In no instance was there any sign of gangrene. Because of the excellent healing of the severed tissues the regeneration of the lymphatics could be studied for probably the first time under what may be considered normal conditions. Moreover, in our procedure the division of all lymphatics to the limb removed the difficulty experienced by Arthur Meyer when he was unable to produce sufficient stasis to demonstrate the regeneration of lymphatic trunks.

LYMPHATICS OF THE EXTREMITY

Normally there are two sets of lymphatics in the extremity, superficial and deep. These arise in the embryo¹⁴ from the primary iliac sacs which are dorsolateral to the aorta. The posterior trunk of these sacs gives off one large branch (the common iliac) which soon breaks into a hypogastric or internal iliac trunk and an external iliac or femoral trunk. The latter drains the two sets of lymphatics from the hind limb. In the embryo the external iliac trunk sends a few lateral branches with the sciatic artery; it then divides into a caudal and a medial group, the latter forming the inguinal lymphatics, which drain a plexus along the inguinal ligament. This plexus is converted into elongated lymph nodes which separate into deep and superficial groups draining the lower abdominal wall, external genitalia, perineum, mesial side of the thigh and practically the whole of the lower extremity. The remaining vessels of the external iliac trunk continue caudally and follow the femoral artery in its course to the thigh. A popliteal gland becomes differentiated and drains most of the lymphatics of the lower leg and foot. The posterior trunk of the primary iliac sacs is differentiated into lymph nodes which are situated about the iliac vessels and the terminal portion of the abdominal aorta.

The lymphatics of the deeper set were first clearly demonstrated by Aagard¹⁵ in 1913. The lymphatics of the muscle and muscle sheaths injected with prussian blue form networks in the muscle sheaths and unite to form larger vessels that drain into the regional lymph glands.

14. Sabin, Florence R.: The Origin and Development of the Lymphatic System, Rep. Johns Hopkins Hosp., 1913. Reichert, F. L.: On the Fate of the Primary Lymph Sacs in the Abdominal Region of the Pig, and the Development of Lymph Channels in the Abdominal and Pelvic Regions, Contributions to Embryology no. 58, 1921, p. 17-39, Carnegie Inst. Washington pub. 276.

15. Aagard, O. C.: Ueber die lymphgefasse der zunge, des quergestreiften muskelgewebes und der speicheldruesen des menschen, Anatomischer heften von Fr. Merkel und R. Bonnet, 1913, vol. 47, pp. 602-620.



Fig. 3.—Cleared specimen of a replanted thigh, showing the regenerated lymphatics in black and the arterial system in white.

In the adult animal, therefore, most of the superficial lymphatics of the leg and foot, as well as some of the deep lymphatics that drain the muscles of the leg terminate in the popliteal lymph gland. From this gland large efferent trunks course along the femoral vessels to end in the external iliac glands just distal to the trifurcation of the aorta. Many of the superficial lymphatics of the thigh and upper leg drain into the inguinal lymph glands which in turn have efferent vessels terminating in the external iliac glands. The deeper set of lymphatics in the muscle sheaths of the thigh eventually enter trunks that accompany the main femoral lymphatics and drain into the large external iliac glands.

METHOD

In the limb replantation experiments it was comparatively easy to follow the regeneration of both the superficial and deep sets of lymphatics. Of the various methods for their demonstration methylene blue and india ink were found to be most satisfactory. Barium, thorium and bismuth, and other substances, by which the lymphatics might well be outlined through the roentgen rays, were repeatedly tried but, unfortunately, no satisfactory technic could be developed for obtaining convincing roentgenograms. The india ink method proved to be excellent not only for dissections immediately after the injection, but also for making permanent cleared specimens. It was thus possible to demonstrate the smallest lymphatic channels.

Several hours before the animal was sacrificed, diluted india ink was introduced into the foot pads and into the skin of the leg and thigh distal to the operative line and also into the popliteal lymph gland. The animal was then killed with ether.

In some cases the arterial system also was injected using the white bismuth roentgen-ray mass of Hill.¹⁶ Unless a dissection was made immediately, the entire thigh and tissues of the pelvic floor, including the pelvic lymph glands, were removed en bloc, hardened in formaldehyde and cleared by the Spalteholz method as modified by Sabin.¹⁷ In these cleared specimens the black lymphatic vessels stood out sharply in the nearly transparent tissue. A striking contrast was presented by the arterial tree outlined by the white bismuth mass and the black lymphatics filled with india ink (fig. 3). Specimens were made at varying intervals (two days to fourteen months) after operation.

16. Hill, E. C.: Notes on an Opaque X-Ray Mass, *Bull. Johns Hopkins Hosp.* 35:218 (July) 1924.

17. Sabin, Florence R.: On the Fate of the Posterior Cardinal Veins and Their Relation to the Development of the Vena Cava and Azygos in the Embryo Pig, *Contributions to Embryology*, 1915, 33, Carnegie Inst. Washington pub. 223.

LYMPHATIC REGENERATION

The earliest specimen showing regeneration of the lymphatics was four days after operation. This regeneration occurred in the superficial set of lymphatics and consisted of three or four areas at the line of skin division where healing was proceeding in the well approximated skin edges. In these few areas, tiny black lines extended from the distal injected lymphatics to the severed skin edge, crossed and converged again to enter a single lymphatic on the proximal side where they continued to the inguinal lymph gland, staining it black. Elsewhere the superficial lymphatics were injected only to the replantation line.

This regeneration takes place first in the superficial set and in the areas of careful approximation of the skin edges with healing by first intention. Where there is any appreciable scar, or where healing has been interfered with by trauma, foreign body or infection, the growth of lymphatics across that region may be delayed for weeks or months, even as Billroth observed years ago in his experiments on the lip. Only after many such replantation operations with utmost vigilance as to aseptic precautions, control of hemorrhage, gentle handling of tissues and careful and accurate approximations—all of these the basic principles of Professor Halsted's teaching—did sufficient operative skill develop for the demonstration of lymphatic regeneration at the early period of four days.

The deep set of lymphatics was first demonstrated to show regeneration in a specimen made eight days after replantation. Both the superficial and deep sets were injected. The intradermal ink injections showed the superficial lymphatic system as tiny tortuous black lines just beneath the skin extending to the line of union of the circular skin closure where, in various areas, arborizations appeared and extended across the wound to form on the proximal side a converging fan of tiny vessels drawn into larger channels to the inguinal lymph glands (figs. 2 and 3). This bridging of the wound by new or regenerating lymphatics occurred at sites where the primary wound healing had the least amount of reaction and scarring. In the deeper lymphatic set the areas of regeneration were not as numerous. From the popliteal lymph gland small black vessels coursed for a distance with the blood vessels. As they approached the replantation line ramifications were found between the muscle groups, in the intermuscular septums, and in the muscle sheaths which finally crossed the wound as minute branches, continued for a distance in the muscle sheaths, then united with others into one or two main femoral lymphatic trunks which emptied into the large external iliac glands. That these iliac glands were not blackened by ink from the inguinal glands was ascertained by injecting only the deep set in another animal.

In specimens in which the lymphatic injections were made from two, three to twenty weeks after replantation the main lymphatic trunks had frequently reunited, occasionally without any evidence of their point of division or else with an irregularity and kinking in the vessels at this point.

In figures 2 and 3 the superficial lymphatic set of an eight day specimen has been added to the drawing which showed only the lymphatics of the deeper set made from the cleared specimen of the left thigh of a dog thirty days after replantation. The black vessels are lymphatics and the arterial system is white, as outlined by Hill's bismuth mass. Some back flow of ink from the iliac glands into a few branches from the pelvic region is shown in the illustration. Adjacent to the trifurcation of the aorta lie the iliac glands darkened with ink. The skin is not included in the drawing but the lymphatics of this superficial group are shown as strong black lines coursing over the popliteal lymph gland, which was injected with ink, to the two inguinal glands. The femoral trunk lymphatics follow the blood vessels to the operative line, but a number of small branches ramify through the deeper intermuscular septums to cross the replantation area where they unite with other deep lymphatics that eventually drain into the iliac gland.

POSTOPERATIVE EDEMA

That the lymphatics play a rôle in the postoperative edema in this type of operation is evident, though it is not possible to determine the relative importance of either the venous or lymphatic systems in its production.

Following replantation, swelling of the limb distal to the suture line begins on the second day, reaches a maximum, as indicated by measurements, on the fourth or beginning of the fifth day, and has subsided completely by the seventh or eighth day. In another report it will be shown that while the growth of the arterial vessels across the operative field occurs about the third day, the venous and lymphatic channels have not regenerated until the fourth day when the subsidence of the edema is just beginning.

The operative procedure has, therefore, disturbed the circulatory balance between the arterial system in the one direction and the lymphaticovenous system in the other. Once the limb has reached its maximum swelling or is just commencing to subside the only patent venous channel, the femoral vein, can be ligated with impunity, since neither gangrene will ensue nor further edema occur. In fact, the delay in the subsidence of the edema will be only one or two days.

From these observations and injections it seems clear that in the fourth and fifth days after replantation the venous regeneration is much

more abundant than the lymphatic, the latter as yet having little effect on the edema.

No change whatever can be seen in the limb if the femoral vein is ligated after seven or eight days, when the subsidence of the swelling has just been completed. If, however, the lymphatics are blocked with india ink granules at this time, the edema reappears. It would seem that the lymphatic system with its regeneration has a relatively important rôle in bringing about the subsidence of the edema at this stage.

Repetition of this experiment several days later, on the tenth and twelfth days, again shows that ligation of the femoral vein leads to no change in the limb distally, nor does blockage of the lymphatic vessels at this time lead to edema. Now apparently the new venous channels are functioning adequately.

PRACTICAL SIGNIFICANCE OF THESE EXPERIMENTS

The importance of the lymphatic system in the spread of cancer cells has been recognized for many years. With this knowledge of cancer extension along lymphatic channels the so-called radical operation was developed in which not only the primary growth but also the adjacent tissue over a relatively large area and the regional lymph glands were removed en bloc.

In certain regions of the body, particularly about the mouth and jaw, some surgeons have divided the operation into two stages. The aseptic part of the operation is done first; namely, the block dissection of the cervical lymph nodes. On the healing of this aseptic wound in one or two weeks, the second stage is performed by either removing the primary growth surgically or treating it with radium.

Although this manner of radical treatment has certain advantages in securing better wound healing, it does introduce the question of possible regeneration of lymphatic channels between the first and second stages. Since it has been shown that lymphatics do regenerate in less than a week such an operative procedure in the radical treatment of cancer would be dangerous.

SUMMARY

Regeneration of lymphatics has been demonstrated under conditions closely approximating the normal. The results are based on injection experiments in replanted limbs of dogs.

New lymphatics are shown to cross a scar as early as the fourth day and by the eighth day the regeneration is physiologically adequate in both the deep and the superficial sets of lymphatics.

Concurrent experiments have shown that compensatory arterial and venous regeneration occur by the third and fourth day, respectively.

Stasis of the lymphaticovenous system provides a stimulus for the regeneration of both groups of lymphatics.

Proof is advanced that the lymphatics play an important rôle in assisting the veins in overcoming edema and restoring a limb to its normal condition.

Study of the postoperative edema following replantation of the limb leads to a better understanding of such postoperative changes as edema and induration of the skin and subcutaneous tissues after dissections of the glands of the neck.

These studies on lymphatic regeneration offer reasons for surgical procedures in treating malignant conditions; namely, the primary growth should be removed before or at the same time as the regional glandular dissection. If, as is sometimes practiced, the clean operation of removal of glands is done a week or more before the primary growth is excised, sufficient time will have elapsed for the regeneration of new lymphatic channels.

INTESTINAL OBSTRUCTION

A SURVEY OF 135 PERSONAL CASES

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The mortality in surgical cases of intestinal obstruction is entirely too high. Reports show that it is 30, 40, 50 per cent, and even higher. There is no phase of abdominal surgery that offers so great opportunity for improvement in its results as that of intestinal obstruction. The mortality in operative cases should not be more than 5 or 10 per cent. In order to obtain this end, no great skill is required, or no expensive outlay in apparatus is demanded. We have only to apply a few simple principles of diagnosis and treatment to reduce the death rate for obstruction of the bowels to one-fourth its present surgical mortality. Seventy-five per cent of the deaths after operation are due to late operations. The fate of the patient is determined by the treatment of the first physician that sees him. Quite invariably the sufferer from ileus sends early for a physician; hence the responsibility for success or failure lies entirely on the shoulders of the medical profession. These patients suffer so severely that they do not delay in seeking relief.

In this article we shall not stress the matter of diagnosis, but rather that of the treatment in the hands of the surgeon after the patient comes to the hospital. However, a few brief remarks in the matter of diagnosis will not be out of place. There are five cardinal points in the symptomatology in making a positive diagnosis of intestinal obstruction:

1. Pain, which is of sudden onset, severe and crampy in character.
2. Vomiting, at first reflex, then due to an overflow from reverse peristalsis (but the diagnosis should be made before this overflow occurs).
3. Blocked bowel, in which it is possible to obtain either fecal matter or flatus by the enema. However, the bowel may move once or twice below the obstruction, but following this there is absolute block of the bowel.
4. Visible peristalsis, which can be seen in the majority of cases early, even three or four hours after the onset of the obstruction. This, when observed, in connection with the other four cardinal symptoms is absolutely pathognomonic. It may require an hour or more of careful watching under a good light in order to observe the peristaltic waves. It is a sign well worth looking for. It is an early, rather than a late sign. It will not be seen after distention has taken place.

* Read at the Pacific Coast Surgical Association Meeting, Del Monte, Calif., Feb. 26-27, 1926, illustrated by motion pictures.

5. No fever. There is generally a wrong impression in regard to the temperature in acute ileus. Of course, just before death, there may be some fever, but for the first forty-eight hours there is no rise in the temperature, at least not over half a degree above normal.

There are other signs, symptoms and methods of making a diagnosis, but they are relatively unimportant, and may only serve to confuse us. These five points we have mentioned are sufficient to make a diagnosis of intestinal obstruction. We believe it is possible to recognize acute ileus with more accuracy than appendicitis, gallstones or gastric ulcer. But in order to have these five cardinal signs and symptoms of any importance there are two vital things that must be constantly carried in mind. First, there shall be no hypodermics of morphine given. The majority of patients with intestinal obstruction have one or more hypodermics of morphine administered them by their physician before they are seen by the surgeon. The use of morphine in these cases renders a positive diagnosis only probable, and will likely delay the operation from twelve to twenty-four hours or longer. Second, the administration of cathartics either by the patient's friends or by the physician is purely barbarous and unjustifiable. Four-fifths of the mortality of operative cases of intestinal obstruction can be directly attributed to the administration of morphine and cathartics. The profession has been altogether too slow to recognize the viciousness of these two classes of drugs in all acute painful diseases of the abdomen. Their exhibition in the cases of intestinal obstruction is deadly. The harm that comes from their use may be well illustrated from our own experience of 135 operative cases of acute ileus. Eighty-four of these patients were referred to us; that is, they were examined by some other physician before they were seen by us. Of these eighty-four, twenty-three died, a mortality rate of a little above 27 per cent. Not all of these eighty-four patients had been given cathartics or morphine, but the great majority of the *fatal* cases had been thus treated. Fifty-one of these were patients that were seen only by my associate, Dr. Moran, or myself before operation. Of these fifty-one, three died, a mortality of 6 per cent. None of these fifty-one had any morphine or cathartics given before diagnosis.

In the year 1925, we had twenty-three cases referred, with only three deaths. This may indicate that if surgeons maintain a campaign of education as to the dangers of morphine and cathartics, it may result in lowering very materially our death rate.

We will omit the discussion of differential diagnosis, and we will not try to solve the problem of what causes death in ileus. In the hands of the average surgeon, if operation is performed early the death rate need not be more than 5 or 10 per cent.

A brief review of the technic of treatment follows: An early operation within the first twelve or twenty-four hours after the onset of the

obstruction is imperative. An ample midline incision, extending from the pubes to above the navel, should be made. Evisceration of the obstructed bowel is quite necessary. This may appear to be a vicious procedure. It is contrary to our previous conception of good abdominal surgery. We have instinctively avoided removing the intestines from the abdominal cavity. We have been fearful of shock. Our anesthetist is frequently asked to note if there is any change in the quality or rate of the pulse while the intestines are eviscerated, as we do it. Rarely does she report any change of any importance whatsoever. The intestines, as soon as they are removed from the abdomen, are kept warm by large, hot, salt napkins (water 110 F.). These salt napkins are constantly replaced as they become cool. Traction on the mesentery is avoided, since it is painful and will cause some shock. With the bowels eviscerated, it is very easy to locate the site and cause of the obstruction. Before operation we make no effort to determine the location or nature of the obstructing cause.

It is immaterial to speculate on where the obstruction is or what is causing it. It is quite sufficient to determine that somewhere by some cause there is a mechanical block of the bowel. We can quickly and easily recognize its site and nature after the abdomen is open. As soon as it is found, the obstruction is relieved. But should we stop here, in the majority of our cases, we have only half completed our task. From causes undetermined, the contents of the bowel are very detrimental to the patient. It seems to be extremely toxic. To leave these imprisoned contents in the bowel is to subject the patient to unnecessary hazard of absorption of toxic material. We must remember that the bowels will not move for perhaps two or three days or more following the operation.

The following is the method that we use in emptying the bowel of its imprisoned contents above the obstruction: We take a large size test tube, with a good flange at the top, and cut off its closed end. Over this is fitted a large rubber tube not to exceed 2 feet in length. At some point in the bowel near the obstruction (just below it if possible) an intestinal clamp is placed. After a purse string Lambert linen suture has been inserted surrounding the site of our intended incision, a longitudinal opening is made into the bowel. We use rather heavy linen for this suture. Then the free end of the test tube is inserted into the bowel, and the purse string suture drawn taut around the flanged end of the test tube. Only the first half of the knot is tied. The suture is then clamped tight to the tube by hemostat. An intestinal clamp is placed distal to this tube. The test tube and the rubber tube connected to it are given to an assistant or nurse. My hands are well anointed with sterile petrolatum. Beginning just as near the upper end of the jejunum as possible, an assistant rapidly pulls the intestines through my petrola-

tum anointed fingers, thus stripping out all of the intestinal contents, which are discharged through the test tube and rubber tube into a basin, held outside of the operating field. The assistant uses gauze in his hands and rapidly draws the intestine through my fingers from the upper jejunum to the test tube. Occasionally we go over these intestines the second time, thus completely removing all contents of the bowel above the obstruction. The intestines are flat, ribbon-like, when we finish. The whole procedure can be done in five or ten minutes. Frequently we are able to take two, three, four or five quarts of foul smelling contents from the obstructed bowel.

The rubber tube connected on the test tube must not be too long. If we have it long enough to reach the floor, we have a siphon effect that will generally aspirate into the tube the opposite wall of the intestines, thus defeating our purposes. By having a short rubber tube, and instructing the nurse to hold it nearly horizontal, we obviate this disagreeable feature.

Emptying the intestine is a life saving procedure in these cases. We may wash the stomach while the patient is on the table—not always, however. Before we instituted this method of emptying the bowel, our patients with obstruction would vomit most furiously for two or three days following the operation. In fact, gastric lavage was the rule every two or three hours and the patients generally looked desperately ill. They were extremely toxic. One would hardly believe the improvement in the general condition of these patients that takes place by simply emptying the intestines, as we have described. We rarely use gastric lavage following the operation, and patients with obstruction have no more postoperative vomiting than an ordinary patient with appendix, gallbladder, stomach or pelvic disease. And their convalescence following operation is as uneventful and smooth as that of any other abdominal surgery. The operation should be done as expeditiously as possible—from thirty to forty minutes is ample time to carry out the procedure that we have mentioned. We use no drainage. Proctoclysis is the rule. Generally, we use salt solution, although if there is any acidosis, which sometimes occurs, we use soda. Morphine may be used postoperatively for twenty-four hours. No cathartic is given at all. The bowels will generally move of their own accord within four or five days after the operation. If they do not, an enema may be used.

Except for cancer of the large bowel, we never use temporary enterostomy. We feel that temporary enterostomy only empties a few coils of the intestines in the immediate vicinity, and the obstruction goes on the same as ever.

This article is based on the experience of 135 operative cases, twenty of these cancer of the large bowel, with seven deaths; thirty strangulated hernias (all varieties) with six deaths; postoperative adhesions (old),

forty-six cases with nine deaths; nine cases of postoperative adhesions (new), that is, those occurring in the hospital before discharge from the hospital, with no deaths (all of these were drainage appendix cases); twelve intussusception cases with two deaths; eight volvulus cases with one death; ten miscellaneous cases with one death; or a total of 135 cases with twenty-six deaths, a general mortality rate of 19.2 per cent.

The fatal cases include, of course, all those in which death occurred in the hospital from any cause whatsoever; also one patient that died of gangrene of the lung three weeks after the operation, ten days after he had returned home, and one patient with abscess of the lung due to an infected emboli from the abdominal wall. This man died six weeks after his operation, and a month after he had left the hospital. So we feel that the mortality rate is an accurate statement of the results.

SUMMARY

No morphine or cathartics should be given to any patient suffering from abdominal pain and vomiting. Pain, vomiting, blocked bowel, visible peristalsis and no fever are the five cardinal symptoms and signs of an obstructed bowel. Operation should be done the first twelve or twenty-four hours. The imprisoned contents of the bowel above the obstruction should be removed. The mortality can be reduced to less than 10 per cent.

By carrying out the principles enunciated here, one need have no more dread of intestinal obstruction than he would of gallstones, ulcers of the stomach or pelvic tumors. The operation and after-care will be no more difficult than in any other abdominal surgical procedure.

THE SURGICAL CONSCIENCE *

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I am deeply sensible of the great honor conferred on me last April at our organization meeting in electing me the first president of this association. I feel that there are many men on this coast who, by virtue of their long service to the profession and because of their contributions to surgery, are better qualified than I for this position, but I am sure there are none who are more sincere in their loyalty to the cause of surgery nor more enthusiastic in their faith as to the possibilities of this organization. I believe it marks an epoch in the development of surgery on the Pacific coast.

I have chosen as my subject for the first presidential address, the surgical conscience.

The all important part played by infection in surgery, as first pointed out by Lord Lister, early focused the efforts of surgeons on the development of aseptic technic. The term aseptic conscience came to have a very definite significance, not alone for surgeons but also for nurses and hospital attendants. It did much toward creating the esprit de corps of the operating room and stimulated all who had to do with surgery to practice that infinite care which we now recognize as necessary to successful surgery and which has become standardized in most hospitals.

The term, which played such an important rôle in the early days of surgery, is now rarely used, so common has the knowledge of bacteriology become and so well established is the theory of asepsis. Operating room technic for which the surgeon formerly felt himself responsible has now been committed largely to the nursing personnel of the operating room. Little is now left for the surgeon in preparing for an operation. Having properly prepared his hands, he enters the operating amphitheater with a clear conscience, confident that every precaution has been taken to prevent infection. He is now responsible for his technic alone. The highly trained surgical nurse has relieved him of all the important minutiae of asepsis. Even his operating technic, so far as asepsis is concerned, is safeguarded by the watchful, unobtrusive nurse who calls his attention to a torn glove, a contaminated instrument or a soiled dressing. We surgeons are prone to forget that much of our success depends on these conscientious, untiring and often poorly rewarded nurses.

* President's address read before the Pacific Coast Surgical Association, Del Monte, Calif., Feb. 26 and 27, 1926.

But there is a much larger moral obligation on the surgeon than that which has to do with aseptic surgical technic as employed in an individual case. It is this larger obligation which I wish to emphasize at this first annual meeting of the Pacific Coast Surgical Association and to discuss under the name of the surgical conscience, the manifold relationships of the surgeon to his patient, his medical colleagues and to the community. I believe that such a discussion if frank and free will be profitable in clarifying our own minds on certain phases of our professional life and that by so doing we may point the way to the correction of some of the evils which have crept into our guild. As a result of these evils, the medical profession has lost prestige in the public mind and there is great danger, if they are not corrected by the profession itself, that it may sink into still lower levels of professional integrity and self respect.

The surgical conscience may be discussed under the following headings:

As related to the necessary preparation for the practice of surgery. Are we not as a profession encouraging half equipped and poorly trained men to undertake surgery? Our medical schools and our state laws, by virtue of their conferring and licensing powers, put the stamp of approval on the young practitioner and he is vested with both moral and legal authority to perform the most difficult and dangerous operations immediately on graduation.

Most of the older members of this association obtained their surgical experience and skill in the hard school of general practice. Few of us, I think, would assert that we have not sacrificed lives that might have been saved had we possessed better judgment and greater skill. This is true notwithstanding the fact that we did the best we could. Surgery has made such rapid strides in the last thirty years that it has been impossible to train men adequately and in sufficient numbers to meet the demands of the public. This necessitated the employment of poorly trained and self made surgeons. The broad background that the surgeons of the passing generation acquired in general practice and their brilliant achievements were in large measure due to their wide knowledge of general medicine.

It is no longer justifiable to rely on private practice for training in surgery; neither should we be satisfied with purely didactic and technical training, such as an apprenticeship in surgery affords. But a wise combination of both will insure the requisite technical skill and surgical judgment that should characterize the surgeon of the future.

There is now a surplus of surgeons in almost every community. Competition is now so keen that ambitious young surgeons with little practice and little experience are finding indications for surgery in a large percentage of the patients who consult them. It is the exception to find a woman over 40 who has not had one or more operations and

I am sure that all of you will testify that much of this surgery is ill advised and poorly executed.

What is the solution? I am not prepared to offer a satisfactory solution but I believe a quickened conscience and a concerted effort on the part of associations such as this can find a remedy. I believe that the ultimate solution lies in a special apprenticeship of not less than five years. The regular medical license should carry with it the right to practice only minor and emergency surgery. The commission on the improvement of medical education which has recently been organized will doubtless have some valuable recommendations to make on educational requirements for specialism. It is to make a comprehensive study of medical education extending over a period of five years and the personnel of the committee insures a comprehensive survey.

The second heading I would suggest for this discussion of the surgical conscience is, the care that should be employed in the selection of cases for operation. In no field of human activity is there greater need for a keen conscience and a trained judgment than in the practice of surgery. The most rigid checks are necessary if the patient is to receive just treatment. This is particularly true in the field of elective surgery. In traumatic and emergency surgery the indications for treatment are fairly definite and there is as much danger of erring on the side of conservatism as on that of radicalism, but in the great field of elective or doubtful cases, this is not so. Too often hasty diagnoses are made on insufficient evidence and too little time allowed for thorough preparation for operation. The surgeon is too often influenced by monetary considerations, by the fear of competition and by the opinions of the patient. Sometimes the surgeon's convenience, his vacation plans, his golf engagement or some other social affair will enter into the decision as to when an operation shall be done and may well be the determining factor in its outcome. Often a desire to save the patient expense and incidentally to conserve his resources so that he can pay a better fee will deter the careless and unscrupulous surgeon from resorting to all necessary diagnostic and preoperative precautions.

Routine preoperative preparation in every major operation, even in those patients who are apparently in good condition, I am sure, is commonly neglected and is the cause of many unnecessary deaths. Take, for example, the large group of cases in which there is a secondary anemia and dehydration. These patients, even to the experienced eye, look pretty well and the average surgeon will advise operation without thought of danger. If the blood is examined it will often show a hemoglobin around 50 per cent. The blood pressure will be 100 systolic, or less. Such a patient will probably survive a skillful, dexterous operation but the margin of safety is very narrow. The same patient after two or three days in bed with daily infusions of 2,000 cc. of salt solution and a 100 cc.

transfusion will so improve that even a blundering operation will be tolerated. The margin of safety can be still further increased by preparing for a postoperative transfusion should undue complications arise or the patient's condition prove unsatisfactory at the conclusion of the operation.

Another group of cases in which the most painstaking care is necessary, both preoperatively and postoperatively, if the best results are to be secured, is that class suffering from partial or chronic intestinal obstruction. Carefully taken roentgenograms to determine the site of obstruction and the amount of stasis, blood chemistry estimations to determine the degree of toxemia, thorough cleansing of the intestinal tract and the restoration of fluids are all preoperative measures of the greatest importance. Then the conscientious surgeon must face the necessity for two or more operations if he is to give the patient the maximum chance for recovery and restore the fecal current. He must be willing to face the criticism of the patient and his friends if a permanent fistula remains and he must have the courage to do no more at each operation than the patient can endure, even though it means weeks in the hospital with troublesome daily dressings, the abandonment of all thought of compensation, and even though a malpractice suit is staring him in the face at the end.

How often have we seen deaths following attempts at complete operations in resecting the bowel for chronic obstruction by inexperienced or conscienceless surgeons! How often have we cherished vain regrets at the fatal outcome of surgical operations or been tormented with the thought that we might have done better had we taken more time to study our cases, given more thorough preparation or exercised more patience and better judgment at the operating table! I believe that all of these factors should enter into the training of young men for surgery and that those of us who have to do with the instruction of these men should lay stress on the necessity of developing a surgical conscience, much as we emphasized in the beginning of the aseptic era the aseptic conscience.

Just as the technic of the operating room typifies the aseptic conscience, so the modern method of handling a severe case of hyperthyroidism typifies the surgical conscience. Here success cannot be cheaply achieved as in abdominal surgery, but the utmost care must be observed in every step of the treatment. Knowledge, skill and a keen conscience are the only guarantors of success. The boldest and most unscrupulous surgeon, the surgeon who would not hesitate to undertake the most difficult abdominal operation hesitates in the presence of such a case. Why? Because he knows that no slap dash methods will avail here. The most painstaking examinations must precede all thought of surgery: repeated laboratory tests, careful blood pressure readings, long

and tedious preoperative preparation, operative procedures planned and executed with the most meticulous attention to detail and the most careful selection of anesthetics. The fear of injury to the laryngeal nerves and parathyroids, the danger of postoperative reactions, the possibility of poor cosmetic results, all of these considerations haunt the careless and inexperienced operator and deter him from hasty and ill advised surgery. Even the remunerative factor is uncertain, for several operations, uncertain results and long delay preclude the expectation of large fees promptly paid. This is the type of surgery that tests the true character and skill of the surgeon. The attitude of mind requisite to success in this field of surgery should be the standard toward which all true surgeons should strive.

In the domain of surgical technic there is need of greater gentleness in handling the tissues and of more painstaking care in eliminating every factor contributing to shock. The use of powerful mechanical retractors, the neglect of hemostasis, the unnecessary bruising of organs and traction on them are all too common. There is need of developing an atraumatic conscience analogous to the aseptic conscience. The true surgeon should shrink from needless trauma as he would from the conscious introduction of infection.

The startling statistics presented by Dr. A. Murat Willis of Richmond at the 1925 session of the American College of Surgeons are convincing evidence that surgical judgment and technic, outside of the great clinics, are still very defective. He showed that in the area of vital statistics the deaths from appendicitis per hundred thousand of population have increased 31 per cent between the years of 1905 and 1922. During the same period there has been a percentage increase of 77 per cent in deaths from gallbladder disease and of 250 per cent in goiter. He did not state that this percentage in deaths from these common affections was entirely the fault of poor surgery, but as these diseases are now treated largely by surgeons it is probable that the rapidly mounting mortality is in large measure the result of injudicious and unskilful surgery. The recommendation of Dr. Willis that a careful survey be made to determine the factors responsible for this increased mortality should have the support of all conscientious surgeons. We as surgeons have flattered ourselves that the treatment of appendicitis was standardized and most of us have thought that the mortality was declining. These facts should awaken us to a new sense of responsibility.

Finally, I wish to discuss the surgical conscience in relation to the fee. I realize that here I am treading on dangerous ground and that I may lay myself open to criticism, but I believe it is incumbent on those of us who are looked on as leaders in the profession to sound a note of warning on this phase of surgical conduct. The division of fees has come to be recognized by all reputable surgeons as a dishonorable and

degrading practice. The American College of Surgeons has done much toward bringing this practice into disrepute. Nevertheless, it is still continued by a large group of surgeons and is defended by some men as justifiable. I believe that any unprejudiced mind will condemn it as demoralizing to both the physician who receives a commission for referring the case and to the surgeon who divides his fee. It converts a professional relationship into a commercial transaction and stultifies the conscience of both parties to it. Moreover, it makes a pawn of the patient and tempts both physician and surgeon to recommend unnecessary surgery. While it is still a great evil, it has been driven into the byways and alleys where the scavengers and highwaymen of medicine lurk.

I believe a greater evil than fee splitting is threatening our profession and this is the practice of charging exorbitant fees. There is a strong tendency toward commercialism among surgeons today and the humanitarian and ethical ideals which have been the glory of our profession are in danger of being submerged. Fees out of all proportion to the service rendered and to the ability of the patient to pay are being charged by surgeons of little training and ability. Indeed, much of the surgery for which these exorbitant fees are charged is poorly advised or unnecessary. Many surgeons of standing and ability, indifferent to every sentiment of fairness and generosity, are exacting fees that savor of rank commercialism. Young men entering surgery are no longer willing to do the drudgery and serve the hard apprenticeship that most of the surgeons of this generation experienced. They expect and demand the same fees as men who have earned their reputations by long and arduous efforts. Few of the younger men are willing to enter general practice and for moderate compensation act as the family adviser in matters of health. The vast majority of our well equipped medical graduates are ambitious to enter the surgical specialties soon after graduation and few of them acquire the broad background which five or ten years of general practice will give. The result of this attitude of mind is that people of moderate means can no longer find competent graduates of regular medicine who are willing to advise them and treat their minor ailments for moderate fees. It is necessary now to consult a series of specialists and incur large bills in order to obtain satisfactory medical service. The growth of cults, free dispensaries and lay movements along medical lines can be largely ascribed, I believe, to this failure of the regular medical profession to meet the needs of the average man. I am not decrying the charging of substantial fees when the patient is able to pay and when real service has been rendered, but the present tendency to emphasize the money making side of our profession should be strongly condemned. When the fee becomes the dominant factor in the practice of medicine and when young men come to regard it as

a money making calling, it has fallen from its high estate and we can no longer boast of the nobleness and sacredness of our calling. Osler once said to a group of students entering Johns Hopkins: "If you look forward to a lucrative practice, go home. But if you enter medicine in exactly the same spirit that the missionary leaves for his foreign field, that is, believing that in medicine you best can use your talents for your fellow men, we welcome you." The commercial spirit is not confined to surgery; every branch of medicine has taken its cue from the general surgeon and all are striving to collect fees commensurate with those of the surgeon. The net result is that medical and surgical fees, plus hospital charges, have reached a point where they are prohibitive for any but the rich. To be sure, the increased cost of living, the expensive equipment and appliances essential to the practice of modern scientific medicine have necessitated an increase in medical and surgical fees, but these increased expenses do not justify the exorbitant charges that many surgeons and specialists are demanding.

It would seem that the wave of materialism which has swept the world, and particularly America, since the Great War, has led to an abandonment of many of our professional ideals. In the words of Wordsworth:

"The world is too much with us: late and soon,
Getting and spending, we lay waste our powers:
Little we see in Nature that is ours;
We have given our hearts away, a sordid boon!"

Surgery because of its spectacular growth in the last twenty-five years, because of its brilliant achievements and its appeal to the popular imagination, has been peculiarly liable to abuses and exploitation. While I believe that the vast majority of surgeons are incorruptible and deeply conscious of their great responsibilities, there is a lure for the unscrupulous, the ambitious and conscienceless to prey on the public and profit by the profound confidence in surgery which has been created by conservative, painstaking, unselfish men.

Human life and humanitarian service cannot be measured by the same standards as those that govern the ordinary transactions of life. No sum of money can be weighed against life and health and when a physician strives to justify himself in charging unreasonable fees by comparing them with the price of a beautiful painting, a piece of property or other chattel, he is lowering his own dignity and degrading a noble profession. These matters cannot be adjusted by fee schedules nor by placing charges on a time basis, but by precept and example the high minded men of the profession can set standards of justice and reasonableness beyond which, by common consent, the dignified and honorable physician will not go. We can have no safer guide for our future con-

duct than the torch which has been handed down to us by the master surgeons of this country. What have been their dominating characteristics? They have been first of all men of broad sympathy and deep insight into human nature. They have been men of indomitable will and untiring zeal. They have been men inspired by the vision of a great mission. They have been just, generous and merciful. They have placed human life above every consideration. They have been good citizens, bearing manfully their part in the stress of war. I trust this association will be instrumental in restoring to the surgical profession that spirit of service and that devotion to science and to the welfare of humanity which characterized the lives and teachings of the great masters of surgery.

THE MECHANISM OF ACUTE BACTERIAL INFECTION OF A JOINT

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NEW YORK

This article will discuss only those cases of acute arthritis (bacterial infection of a joint) which are caused by the ordinary forms of pyogenic bacteria, staphylococci and streptococci. Cases due to infection by tubercle bacilli, syphilitic virus or actinomyces are not included; nor any case originating in any extraordinary pathology such as that associated with thrombo-angiitis obliterans or senile vascular gangrene; nor cases of joint infection complicating the forms of gangrene associated with diabetes mellitus. Cases corresponding to obscure etiologic factors, such as those commonly known as arthritis deformans, metabolic arthritis and gout, are also not included in this article.

The old terminology used in association with the phenomena of bacterial infection and including such terms as sepsis, septicemia, sapremia and pyemia will not be employed here. The reasons for this were given in a previous article and a simplified terminology was suggested. Here only the terms infection, bacteriemia and general blood infection will be employed, with the following definitions:

1. The term infection will be used as a generic one and will include all the phenomena of a bacterial attack on tissue, organ or the entire body. The various kinds of infection will naturally be described in accordance with the tissue, the organ, or the part of the body involved, and in accordance with the organism or organisms encountered; e. g., saprophytic infection of the uterus, staphylococcus infection of the skin or streptococcus infection of the liver. When no other modifying term is employed it is to be assumed that cultivations of the peripheral blood taken during life are sterile. The differentiation commonly made between local and general infection theoretically does not exist and the terminology is one more of convenience than of accuracy. Local infections must necessarily involve some degree of general constitutional reaction and general infections must necessarily find their beginnings in or be associated with a local focus of infection. As far as possible this differentiation will be avoided or made clear in the text whenever it must be used.

2. The term bacteriemia will also be used in a generic sense to indicate any condition in which living bacteria can be cultivated from the peripheral blood during life. The various kinds of bacteriemia will naturally be described in accordance with the organism; e. g., staphylococcus bacteriemia, streptococcus bacteriemia.

3. The term general blood infection will indicate a subgroup of the generic term bacteriemia and in this article a distinction will be made between the terms bacteriemia and general blood infection on the following basis: The term bacteriemia is meant to imply a condition in which the organisms demonstrable in the circulating blood by the usual cultural methods are derived from a local lesion somewhere in the body; they are usually small in number, and the faculty of destroying the circulating bacteria is more or less retained by the appropriate antibodies of the blood. The term general blood infection is meant to imply a condition in which in addition to the foregoing a multiplication of the bacteria takes place in the circulation and the faculty of destroying the circulating bacteria is more or less lost by the appropriate antibodies of the blood.

Under appropriate circumstances both of these groups of terms will be employed together, e. g., staphylococcus infection of the skin with staphylococcus bacteriemia or general blood infection. The character of the local lesion in the complete development of any individual infection is best described by the use of the terms primary or secondary (metastatic, subsidiary); thus, primary staphylococcus infection of the skin with staphylococcus bacteriemia or primary streptococcus infection of the tonsil with secondary streptococcus infection of the appendix. The absence of any descriptive bacteriemia indicates that a cultivation of the peripheral blood made during the course of the illness remained sterile.

Acute bacterial infection of a joint finds its origin in many widely differing etiologic factors. In a general way the cases tend to conform themselves into the following groups: (1) those associated with extrinsic causes; (2) those in which the arthritis results from a lesion in its immediate environment, usually by the spreading of a focus of infection; (3) those occurring during the course of a temporary or permanent bacteriemia and in which the joint lesions form metastatic foci.

GROUP 1

A. In civil life bacterial infection of a joint can follow penetrating wounds of all kinds, stab wounds, gunshot wounds, etc. As a general rule these forms of joint infection, if promptly and properly cared for, become restricted to the area of tissue destroyed or in and to the path of the penetrating object, and the results of the injury and the subsequent area of infection are at a minimum when compared with the injury. When neglected or when efficient treatment is not promptly possible, the most extensive process can develop, even to subsequent complete disorganization of the joint and a complete loss of function.

Military wounds follow penetration by missiles of all kinds. These injuries follow along lines similar to those in civil life. The intensity of the infection is usually much more marked, and when combined with the lowered resistances produced by the hardships of modern war-

fare and with the uncertainties and vicissitudes of efficient medical aid under military conditions a greater proportion of cases result in which the excellence of the final result does not approach the ideal looked for in civil practice.

B. Infections of a joint follow compound fractures extending into the articular surface or compound dislocations. In military wounds the track of a missile need not necessarily lie through the joint; in its passage through the bone the resulting comminution is frequently amply sufficient to create an opening into the joint. The end-result depends primarily on the promptness and efficiency of the first aid treatment, and on the extent of actual destruction of the various tissues going into the formation of the joint. Except when the wounds are thoroughly ground with dirt, mud or grease, the amount of permanent infection is relatively small, even though the original contamination is relatively large.

GROUP 2

A. In instances of acute osteomyelitis, I have frequently observed the focus of infection spreading into a joint. The mechanism of this secondary involvement is a threefold one.

(a) In many of the cases the infection travels into the joint through the lymphatic channels. Under such conditions an effusion of serous fluid occurs in the joint, which at first is free from organisms but in which organisms can presently be demonstrated. Actual suppuration follows unless because of efficient treatment or other apparent or obscure cause the original focus begins to retrogress, becomes localized and goes on to cicatrization. Sometimes the joint effusion stops just short of the bacteria carrying stage and after remaining so for a variable time it eventually disappears spontaneously. Small "sympathetic" effusions of this kind quite commonly accompany foci of osteomyelitis which are quite close to a joint.

(b) In a focus of infection in the bone near the joint surface, it can happen that the gradual extension of the infection in the cancellous and cortical tissue results in more and more destruction of bone until a tract forms leading into the interior of the joint. I have been able to demonstrate this lesion several times during the course of an operation. The clinical course suggests that in some of the cases the bone lesion is a relatively minor one and had, perhaps, preexisted for some time, and that an acute rupture takes place into the joint with the sudden development of high fever, with or without chills, and other signs of an acute infection of severe grade. Positive blood cultures are common under such conditions. Commonly the bone lesion is not recognizable in the clinical picture; the arthritis is dominant. In other cases the development of the bone fistula into the joint is a gradual one and is not accompanied by signs of an acute new lesion, or of the exacerbation of a previously existing one; frequently, indeed, the arthritis is seen to develop slowly

during the course of the postoperative dressings on an osteomyelitis wound nearby. In some of these cases it is possible to demonstrate at operation that the bone tissue intervening between the joint surface and the bone focus is carious, by the ease with which an ordinary probe can pass through it and by the macroscopic and microscopic appearances of the tissue.

(c) Abscesses in the soft parts resulting from an acute epiphysitis or an acute osteomyelitis also can convey their infection through the lymphatics and so involve the joint. During the course of an operation I have, on several occasions, been able to pass a probe from an extra-articular abscess directly into a joint. As will be pointed out later, perforation of a suppurating joint also can occur and the end-result would be indistinguishable from a lesion resulting from the perforation of an external abscess into the joint. However, in my experience, several of these were distinctly subperiosteal types of abscesses and for that reason I am of the opinion that the direction of the perforating process was inward into the joint.

I have also seen sympathetic effusions in joints which were contiguous with soft tissue abscesses and which were entirely unrelated to any infection in the bone. It has sometimes been difficult to make sure that a pyarthrosis did not exist, but, invariably, proper incision and drainage of the extra-articular focus of infection has been immediately followed by the retrogression of the joint effusion.

REPORT OF CASES

CASE 1.—A young child developed a focus of infection in the general neighborhood of the right knee, with complete loss of function in the joint. It was difficult to decide whether the infectious process had involved the knee. Incision demonstrated an extra-articular abscess leading from the epiphyseal line and the latter was readily demonstrated in the bottom of the wound. There was an uneventful convalescence and healing with no further progression of the focus of infection and with total restoration of function.

CASE 2.—A patient died with the clinical picture of a general blood infection in which a local focus was present in the neighborhood of one knee. Aspiration of the joint yielded a straw colored fluid which was bacteriologically sterile. Necropsy showed a focus in the lower end of the femur and a joint effusion. This was a "sympathetic" effusion.

CASE 3.—In a young child an amputation of the lower extremity was done through the middle of the thigh for an osteomyelitis of the lower end of the femur with symptoms of general infection. The specimen showed a previously done osteotomy at the outer side of the femur; the soft parts were inflamed and somewhat gangrenous; the bone cavity was ragged but apparently in fair condition.

The knee joint was relaxed. The synovial membrane was red and inflamed and had the appearance of unhealthy granulation tissue. The cartilage was not

eroded, but there were inequalities in places especially toward the condyles. There was no fluid in the joint. The crucial ligaments were covered with similar unhealthy synovial membrane and were soft and relaxed. In the notch, the bone tissue was bad, this corresponding to the under side of the femur. The operative cavity in the femur extended to within one-eighth inch (0.3 cm.) of the joint surface; the intervening bone tissue was diseased and carious, but there was no gross perforation. The epiphyseal cartilage had for the most part disappeared.

The accompanying drawings of the various roentgenograms that were taken at intervals demonstrate the development of the arthritis (Fig. 1, A, B and C).

CASE 4.—In 1898 a man developed an osteomyelitis of the femur. Following operation, healing took place and became permanent and there were no recurrences for the next twenty-three years.

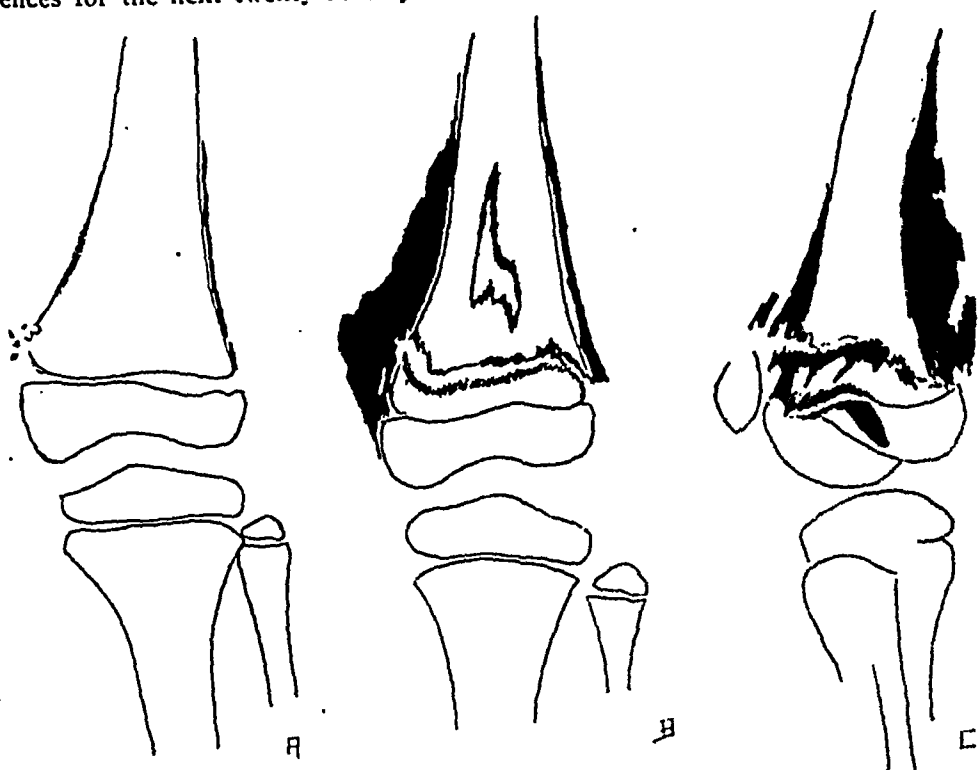


Fig. 1 (case 3).—Tracings from roentgenograms made at progressive intervals of the development of the focus of infection; the figures illustrate the paucity of roentgen-ray evidence of the extent of the final lesion, the method by which the joint becomes involved, and the final degree of destruction.

In 1921 there was a sudden exacerbation of symptoms referable to the site of the previous operation and especially to the knee. At operation suppuration was found in the medullary cavity; the latter was opened to its full extent; the knee joint was not disturbed.

Following this, an abscess developed in the quadriceps bursa from which a thin yellow fluid containing *Staphylococcus aureus* was obtained. Abscesses developed later in the thigh and in the calf of the leg. All of these were properly incised but without getting to the bottom of the trouble. Finally, the whole focus of infection was exposed and it was demonstrated that a sinus existed through carious bone and leading down into the knee joint. The whole outer side of the lower end of the femur was involved in the process as w

as the upper end of the tibia; the joint was thoroughly disorganized. The disease was eradicated as completely as possible and the resulting wound was packed wide open.

Even this was not followed by an arrest of the symptoms and it appeared as if an amputation would be necessary. As a last resort a Mayo arthrotomy was done, and was followed up by a resection of the joint. Thereafter control of the process was obtained and, eventually, healing took place with the development of a stiff knee.

Undoubtedly in this particular instance, the acute exacerbation of symptoms was due to a slow progression of the original bone process and to a relatively acute perforation into the joint.

CASE 5.—An osteomyelitis of the radius was eventually followed by involvement of the joints at either end of the bone. The course of affairs is amply shown in the drawings of the roentgenographic studies that were made at intervals.

B. Instances of joint infection, more commonly than one ordinarily would suppose, follow the accidental and unintentional opening of the joint capsule during the course of a bone operation for such conditions as osteomyelitis, epiphysitis or bone tumor. This mechanism probably accounts for many of the cases of involvement of a joint which are seen to develop after operation and during the subsequent dressings, and for much of the fever which in many of the cases follows an apparently efficient operation and for which an adequate cause is frequently temporarily not demonstrable.

C. Operative intervention is sometimes followed by involvement of a contiguous joint in which the mechanism is an entirely different one. During the radical osteotomy necessary for the eradication of a focus of osteomyelitis, it is possible either to destroy a large branch of the nutrient artery either directly in the manipulations or by a later spread of any thrombotic process which is present as a result of the operative trauma. When opportunely placed the resulting sequestration may take place either wholly or partially within the confines of a joint; involvement of the latter naturally occurs immediately. The notes of the following case illustrate this possibility very accurately.

CASE 6.—A man entered the hospital with a chronic osteomyelitis of one femur, with fistula formation. At the radical osteotomy that was done, it was necessary to go up into the greater trochanter and somewhat into the neck of the bone in order adequately to remove the diseased tissue. After the operation the patient developed great pain in the hip which persisted for several months before it subsided. The course of events is well shown in the drawings of the roentgenograms which were taken at intervals and which are reproduced here. These show that a large sequestrum had formed and separated out of the bone, which included a large part of the neck of the femur; an arthritis developed coincidentally which lead to a disorganization of the joint, to a subluxation and eventually to a fixation of the femoral head in an abnormal position. It is not possible to explain this arthritis except on the basis outlined in the text of this article (Figs. 2 and 3).

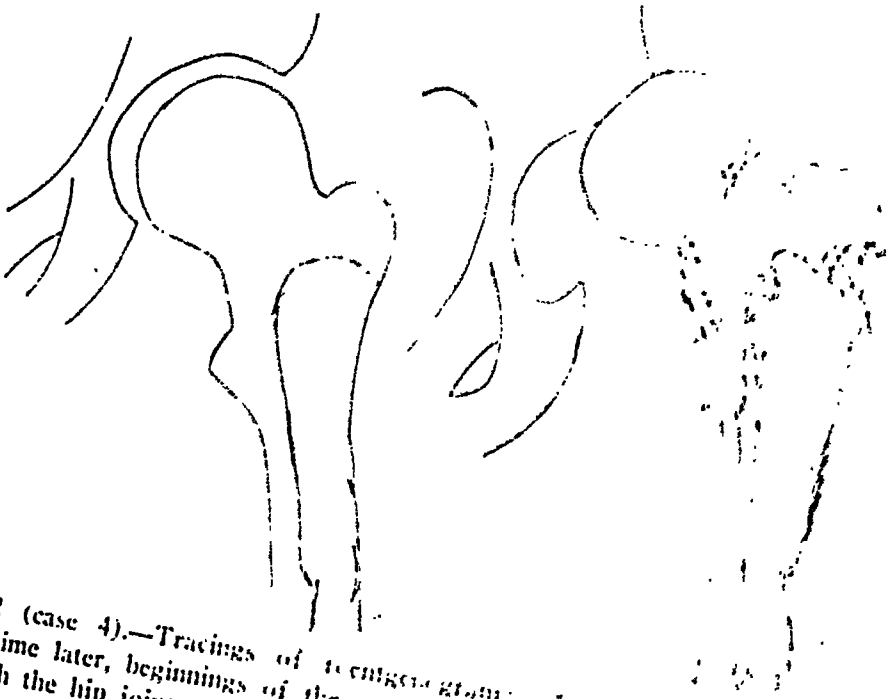


Fig. 2 (case 4).—Tracings of roentgenograms. A, extent of infection; B, some time later, beginnings of the separation of the acetabulum, and extent with which the hip joint was involved in the focus of infection.

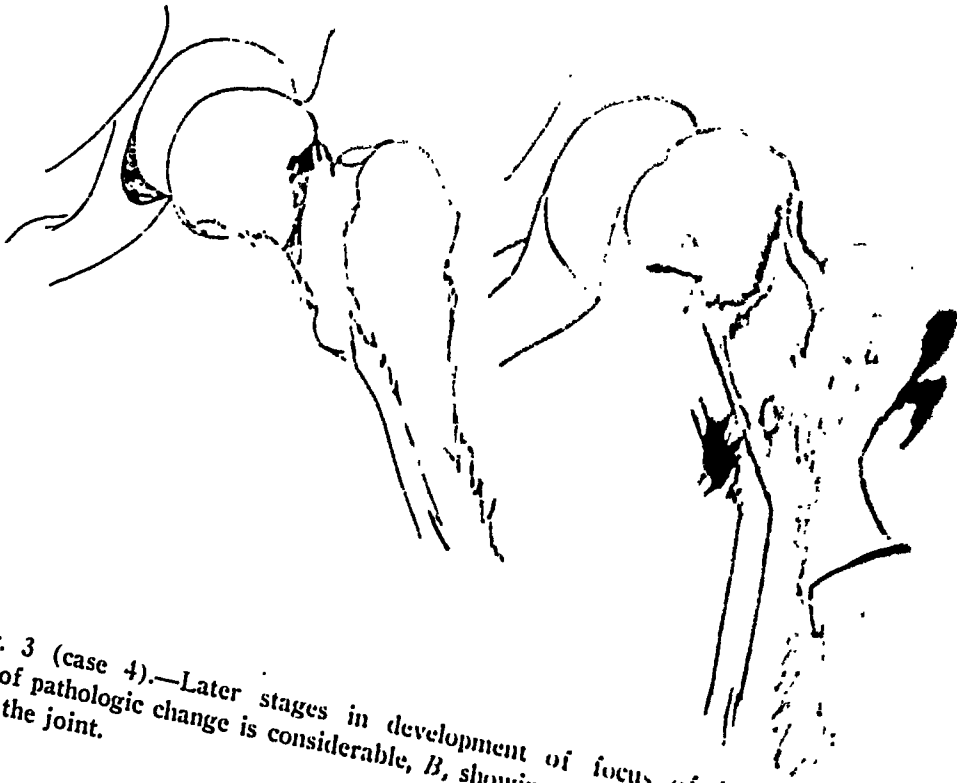


Fig. 3 (case 4).—Later stages in development of focus of infection; the extent of pathologic change is considerable, B, showing the complete disorganization of the joint.

GROUP 3

The most important group of cases of joint infection are those which take place as a result of a hematogenous infection. In previous articles the mechanism of bacteriemia was discussed as it forms the most important single cause in the production of acute osteomyelitis in civil life. A similar mechanism takes place with joint infections of a hematogenous origin. For purposes of clarity the essentials of this mechanism are reiterated as they apply to cases of joint infection.

The ordinary case of acute metastatic bacterial arthritis results from a bacteriemia or general blood infection, the origin of which is in the greatest number of cases obscure. In these cases it is thought that the entry point of the infection must necessarily be some surface (skin or alimentary canal) of the body; in actual practice it is assumed that, with few exceptions (genito-urinary infections, furuncular infections of the skin) this surface is the mucous membrane lining of the alimentary canal at points where collections of lymphadenoid tissue are especially prominent (tonsils, especially; Peyer's patches, etc.). At the latter areas a lesion need not necessarily be demonstrable. In a small minority the bacteriemia or general blood infection accompanies or follows a definite entity such as a pneumonia; or a definite focus of infection is present somewhere in the body—a phlebitis, a postpartum sepsis, a furunculosis—to which the bacteriemia or general blood infection is subsidiary and through which in turn the arthritis originates.

In any case the focus in the joint is a fixation point to which the bacteria circulating in the blood are attracted. Commonly there is a single one of these fixation points following which only a single joint becomes involved. But just as often there are more than one of these foci developing either simultaneously or subsequently to each other. When the number of subsidiary foci is more than one some of the fixation points may be located in other tissues and structures, as, for instance, in a bone or in the fascial planes in the musculature of a limb. Under appropriate circumstances previously described which depend altogether on the character and the physical results of the inflammatory process developing at the fixation point, the latter, in turn, forms a point of distribution from which a bacteremia or general blood infection may occur, and from which subsidiary foci can develop in exactly the same way.

There is no experimental or other evidence that helps in classifying multiple foci developing during the course of any infection. It is perfectly possible for the primary lesion to father every secondary or subsidiary focus that may ever develop, and, on the other hand, it is just as possible for any secondary focus to, in turn, form a point of distribution.

The bacteriemia through which joint infections become established and develop are not always demonstrable. It is well known that these

states may be of temporary duration and the presence of bacteria in the circulating blood even for a short period is sufficient to infect any local area. It is thought that temporary states of bacteriemia are constantly occurring even in conditions of health, and that the natural forces of the body are amply sufficient to overcome these so promptly that no evidence of them is perceptible in any way. It is also known that during the dressing of any wound, more so, perhaps, with a wound of bone, bacteria may be pushed into the circulation so that a temporary bacteriemia is present; this ordinarily lasts only a few hours, is occasionally demonstrable, and has no clinical signs or demonstrable effects.

While in extraordinary circumstances bacteria can pass through a surface of the body (the tonsils, for instance) and multiply in the blood, the available knowledge seems to show that ordinarily bacteria circulating in the blood depend for their existence there primarily on the presence of an infected thrombus. The course of events is one of two: 1. Microscopic pieces of the thrombus carrying a number of living organisms break off and circulate through the blood stream until they are disposed of in some way. Sometimes isolated organisms growing on the surface of the thrombus or groups of them in the forms of bacterial emboli are cast off into the blood stream without any particle of the thrombus itself coming away. Clinically, this is a bacteriemia, as previously defined. Fortunately, in most of these instances the natural antilobes destroy the organisms as fast as they are discharged into the circulation and no subsequent effect is noted. In the minority an infected embolus caught into the capillary network of some tissue and held there becomes a fixation point and furnishes the initial stage of a focus of infection. The fact that fragments of the original embolus, after it have been arrested in bone tissue, or of its secondary thrombus thereafter may, in turn, break off and circulate in the blood furnishes the physical basis for the occurrence of secondary points of distribution. This explains the statements made in the previous paragraphs. 2. In addition to the preceding, the virulence of the bacteria may be sufficient to enable them to multiply in the blood stream.

The physical characteristics of the infected thrombus-embolus formation (fixation point) and its resultant effects on the tissues, bone, cartilage capsule, etc., entering into the structure of a joint and the multiplication of bacteria in the blood stream have direct effects on the clinical picture as regards the association of a bacteriemia.

It is necessary to appreciate the fact that in many of the cases of joint infection, an osteomyelitis of greater or less grade is also present; many times the latter holds the dominating part in the clinical and pathologic anatomic picture. Doubtless many of the facts and phenomena of infection, as related to an arthritis, previously and to be presently discussed, especially those related to the demonstrable presence of bacteria

in the circulation, are many times due to a coincidence of the osteomyelitis.

In actual practice it is found that cases of bacterial infection of a joint can be of three clinical varieties:

1. In the first variety a focus is present in one of the joints with well marked local signs and symptoms but without any clinical signs of a general blood infection. A bacteriemia is not present. The physical basis for this variety lies (a) in a primary and temporary bacteriemia; (b) in the development of a fixation point in a joint, and (c) in the subsequent spontaneous disappearance of the bacteriemia.

2. In the second variety, a well marked focus is present in one of the joints with abundant local signs and symptoms and, in addition, there are clinical indications of a bacteriemia as evidenced by the general signs and symptoms and by the demonstration of living bacteria in the blood stream. The physical basis for this variety is the presence of an infected thrombus-embolus formation which serves to keep up a demonstrable bacteriemia by constantly feeding into the blood stream a comparatively small number of viable organisms. Most commonly, after efficient surgical treatment, the bacteriemia eventually disappears and a recovery is made. It must be remembered that any of these cases may at any time pass into the third group.

3. The clinical picture of the cases in this group is that of a profound general infection: there is a marked toxemia. A local joint focus is either not demonstrable at all because of the paucity of local signs and symptoms, or because the latter are hidden in the profound intoxication; or, if present, the local lesion is easily recognized as being of no consequence in the total clinical picture. The physical basis for the clinical picture lies in an extreme and severe general blood infection with highly virulent organisms in which the bacteria are rapidly multiplying in the blood stream and because of which the subject is rapidly being overwhelmed by a tremendous intoxication. The presence of the infected thrombus-embolus formation forms a negligible factor and the few organisms that are derived from this source play only a primary and inciting part in the production of the bacteriemia; the subsequent multiplication in the blood stream depends on other factors, the most important of which lie in the high virulence of the infecting organism and in the poor resistance of the subject. An endocarditis is usually found under these conditions. In this variety the local point of fixation plays no rôle in the production of any part of the clinical picture. Usually the pathologic anatomic picture is not in an advanced stage at the time the lesion is exposed, either on the operating table, or, as more commonly happens, in the necropsy room.

In actual disease it seems certain that the cases differentiated in these groups each form progressive stages from the next preceding group. A

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3. The clinical picture of the cases in this group is that of a profound general infection: there is a marked toxemia. A local joint focus is either not demonstrable at all because of the paucity of local signs and symptoms, or because the latter are hidden in the profound intoxication; or, if present, the local lesion is easily recognized as being of no consequence in the total clinical picture. The physical basis for the clinical picture lies in an extreme and severe general blood infection with highly virulent organisms in which the bacteria are rapidly multiplying in the blood stream and because of which the subject is rapidly being overwhelmed by a tremendous intoxication. The presence of the infected thrombus-embolus formation forms a negligible factor and the few organisms that are derived from this source play only a primary and inciting part in the production of the bacteriemia; the subsequent multiplication in the blood stream depends on other factors, the most important of which lie in the high virulence of the infecting organism and in the poor resistance of the subject. An endocarditis is usually found under these conditions. In this variety the local point of fixation plays no rôle in the production of any part of the clinical picture. Usually the pathologic anatomic picture is not in an advanced stage at the time the lesion is exposed, either on the operating table, or, as more commonly happens, in the necropsy room.

In actual disease it seems certain that the cases differentiated in these groups each form progressive stages from the next preceding group. A

case in group 1 may pass into group 2; and, conversely, a case in group 2, having been appropriately treated, may retrogress into group 1 as it proceeds to healing and recovery. These interchanges are constantly occurring in clinical surgery. A case in group 2 may pass into group 3, as previously noted; usually under such conditions there is a continued progression until the eventual fatality. In actual practice cases in group 3 must necessarily first pass through the stages indicated by groups 1 and 2; the time interval may be so short, however, owing to the virulence of the infecting organism, or the relative nonresistance of the subject, as to make these stages unrecognizable. One can explain the cases that apparently begin with the characteristics of the cases in group 3 in this way. In many cases characteristics can be distinguished which belong to both group 2 and group 3, and so far as any case partakes of characteristics not belonging to its group, it differs in its clinical manifestations. I have never seen a case in group 3 retrogress spontaneously into group 2; it seems almost impossible to believe that such retrogression can ever occur. It is often a matter of great difficulty, clinically, to make correct judgments as to the coincidence or the absence of an osteomyelitis with an acute joint infection, as to the relative dominance of the one over the other part of the total clinical picture and as to the relation of either of them to an accompanying bacteriemia. This is an especially great difficulty in the most severe cases of group 3, even though in these cases a fatality is always to be expected and the differentiation would, therefore, be of no practical moment.

In the milder cases, much depends on a judgment of this kind as far as operative indication is concerned; for in the acute joint infections with osteomyelitis and positive blood cultures, it is essential to clear out the bone focus immediately, while in pure joint infections with positive blood cultures and no bone involvement a more conservative policy is many times permissible and perhaps even advisable. Bacteriologic studies are frequently of help here; if *Staphylococcus aureus* is demonstrated in the peripheral blood, the chances are much more in favor of an osteomyelitis also being present and the mere demonstration of the organism is frequently an indication for operation. In the presence of streptococci or pneumococci, the chances of bone involvement are at a minimum and operation is usually deferred or not done at all as no bone involvement is expected under these conditions.

In actual disease the occurrence and position of secondary or subsidiary foci (fixation points) depend a great deal on the physical characteristics of the blood vessel network of the individual structure or organ involved. In joint disease this must necessarily include the blood vessel network of the bone and cartilage entering into the joint structure as well as that of the joint capsule and the synovial membrane.

A typical specimen of the circulation in a long bone is shown in figure 2, *A*. There is a separate circulation for the diaphysis and for the epiphysis. The circulation of the epiphysis enters most often at more than one point, though often a main channel can be distinguished. The circulation of the diaphysis is derived from a large vessel, the nutrient artery of the bone which enters a little to one side of the center of the shaft. Immediately, the main vessel divides into a number of large branches which pass, some of them upward and some of them downward toward either end of the shaft. A diffuse network is formed which supplies the entire interior of the bone and its medullary cavity. Toward the end some of the main branches become end vessels. There is a free anastomosis between the plexus of vessels thus established and the vessels derived from the periosteum through Sharpey's fibers. In a growing bone, with the epiphyseal cartilage still present, there is little direct anastomosis between epiphysis and diaphysis and a relative avascular area results; in a fully grown bone there is an extensive anastomosis between the two.

The blood supply of joints in general is not subversive of any classification. The blood supply is derived from a variable number of large vessels in an irregular manner. It then enters the joint by a number of derivative vessels and after perforating the capsule at various places divides and supplies the joint interior. There is a minimum of blood supply in the synovial membrane and practically none in the cartilaginous tissue; both these elements derive a great deal of their food supply through the lymphatic circulation.

A fixation point is formed by the arresting of an embolus (or by a thrombus formation) at some point of this vascular network either in the bone or other joint structures. The actual point depends more on chance than on anything else and is decided by the physics of the local bone or joint circulation at the given moment. Various pathologic pictures result, depending on the size of the plugged vessel, the relative position of the plug, the powers of vascular anastomosis, etc., in conjunction with the character and virulence of the bacteria giving rise to the infection. The dominant characteristics of the pathologic pictures are: (1) a thrombo-arteritis or thrombophlebitis, and (2), in the cases with osteomyelitis, a necrosis of bone and cartilage cells consequent to the disturbance of circulation. The physical characteristics of the pathologic picture depend to the largest extent on the second factor.

The peculiarities of the local capillary circulation at the given point determine whether the confines of the metastatic focus of infection shall be limited entirely to bone or entirely to the joint or whether a simultaneous involvement of both bone and joint shall take place. The anatomic possibilities find their examples commonly in clinical practice and can be grouped as follows:

1. When the fixation point for the thrombus-embolus formation is somewhere in the confines of the soft structures of the joint, the resulting pathologic process is limited to the interior of the joint and passes through the stage of a serous sinovitis to that of a frank suppuration. If regression begins at this point, either spontaneously or after surgical incision, the end-result may be perfect or one approaching the ideal. Should, however, the progress continue or the infection spread to or originate in other structures of the joint, especially bone and cartilage, there must necessarily be structural change in the joint and a corresponding eventual interference or abnormality in its anatomy and physiology.

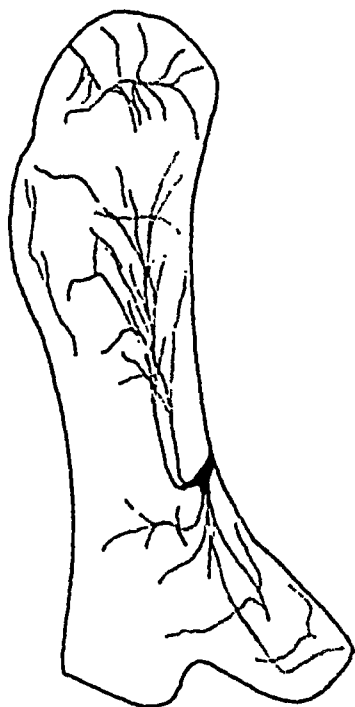


Fig. 4.—Scheme of blood supply of typical long bone obtained by injection with a medium opaque to the roentgen ray (from "Untersuchungen über Knochenarterien" by E. Lexer, Kuliga and Türk).

Simple joint infection of this kind is most apt to occur when the inciting organism is the pneumococcus or a closely related strain of the streptococcus group. The notes of the following case serve as an illustration:

CASE 7 (Alexander).—Ten days before admission to the hospital the patient developed a pharyngitis. This was followed by indefinite wandering pains in a number of the joints, and there was irregular fever of a more or less intermittent type. Finally pain developed in the right ankle, became aggravated and persisted, and there was fever ranging to 104 F. The tissues around the ankle became reddened and tender and there was total loss of function. Incision demonstrated a thick greenish pus in the ankle joint and the neighboring joints of the tarsus. *Pneumococcus I* was cultivated from the pus.

There was an uneventful convalescence following incision. No evidence was present to make one suspect bone involvement. At the time of discharge from the hospital full function had been regained.

2. In children (and young adults) the fixation point is commonly in an epiphyseal line. A number of possibilities result, depending on the relation of the epiphyseal line to the interior of the joint capsule and to the line of reflection of the synovial membrane. Anatomically, the epiphyseal line has a variable relation to the joint interior, depending on the physical structure of the individual joint: in some of the joints the line lies altogether outside the joint; in others it lies outside the joint only partially; in still others it lies altogether within the joint. The observable clinical possibilities are as follows:

A. An epiphysitis develops with or without abscess formation, and during the entire course of the infection there is no demonstrable evidence pointing to involvement of the joint. The physical basis for this naturally lies in the location of the fixation point in an epiphyseal line which is entirely outside the joint.

B. An epiphysitis develops with or without abscess formation and the clinical signs of joint involvement come only later. If this should appear before any operative incision, it indicates that the fixation point was originally situated in a part of an epiphyseal line which was outside the joint and that joint involvement took place, because of the spread of the infection along the epiphyseal line into a portion of it which lay within the joint or because secondary sequestration opened a path into the joint. If the signs of joint involvement come after incision, the possibility is always present that the latter was due to the operative intervention, either accidentally or, perhaps, purposefully.

C. An acute joint infection develops and at operation it is possible to demonstrate a focus of infection in an epiphyseal line in the interior of the joint. It is immaterial whether the given epiphyseal line lies wholly or partially within the joint; the focus of infection is in that part of it which lies within the joint.

3. The anatomy of the interior bone circulation has been discussed exhaustively elsewhere and has been referred to previously in this article. The mechanism of infection limited to the bone was also discussed fully at that time and needs no repetition. Suffice to say here that the fixation point in the vascular network of the bone may be so situated that the focus of infection resulting therefrom may lie at least partially within the interior of the joint. An arthritis coexists from the beginning. In children this, of course, includes the commonly seen epiphyseal infections.

4. It is, of course, perfectly possible for both bone and joint to be simultaneously involved because of the formation of more than one fixation point. I am convinced that this is a common occurrence.

In actual disease the position of fixation points is probably determined by some kind of local trauma at the given point. This has been referred to on a previous occasion. I include under the general term of trauma all varieties, mechanical and physical trauma, chemical trauma. In clinical experience the cases group themselves into (a) those in which there is a distinct history of a definite physical trauma and (b) those in which no such history is elicitable.

A. Cases in which the trauma is a distinct physical entity are, of course, common. I give the notes of one case in which the sequence of events is suggestive.

CASE 8.—A man sustained a fracture of the olecranon process of the ulna. The healing was marked by marked disability and by a later development of fever. Eventually this was proved to be due to a suppurative arthritis of the elbow. It is probable that the joint infection took place through the medium of the fractured bone.

This is an extreme case of trauma. There are many other cases in which the degree of the trauma and its extent varies all the way down to minor grades and until it is so slight as to be barely, or not, recognizable.

The physical basis for this consists of a hematogenous infection in a gross or microscopic hematoma associated with blocking of the circulation at one or more points because of the tearing of the vessels: this is a fixation point for any bacteria carried in the blood stream.

There are other cases in which trauma occurs accidentally during the course of a well established bacteriemia. In cases of general infection the mildest trauma is almost certain to be followed by local infection. In many cases the trauma is so slight as not to be recognized.

B. This group includes all the cases in which there is no history of trauma. Undoubtedly in some, at least, of the cases in this group, trauma was present but passed unnoticed, most probably because of its slight degree or because of some other undiscoverable cause.

It is possible that in some of these cases a certain form of negative or passive trauma is produced by a temporary disturbance of the capillary circulation in a circumscribed area leading to a temporary localized anemia. This might conceivably be produced by a fragment of blood clot, which, having become dislodged at some other distant point, becomes caught in the capillary network of some joint structure. Necessarily the embolus need not carry bacteria, but, once having become arrested in its circulation, it furnishes an ideal environment for the attraction of organisms circulating in the blood.

Circulatory changes which cause changes in nutrition are the physical basis for the "chemical traumas" that I previously mentioned. Many cases with no definite etiologic history of trauma undoubtedly have this form of trauma as a contributing cause.

From what has been said heretofore, it must be apparent that in any given case the presence of a bacteriemia can be referred (1) to the primary lesion; (2) to its secondary focus in the joint; (3) to the presence of another subsidiary focus (bone or other) which by itself is capable of creating a bacteriemia; (4) to the presence of a bacterial valvular lesion, and (5) to the presence of some unrelated complication capable itself of giving rise to a bacteriemia or general blood infection. In any given case it is always important to be able to classify properly the bacteriemia demonstrable. The clinical possibilities are the following:

1. In many of the cases a focus of infection is demonstrable in only one joint. In most of the cases in this group the comparatively small number of bacteria demonstrable in the blood circulation (plate culture method) indicates that the bacteriemia results from the demonstrable local lesion. If, following an adequate operation, the blood becomes sterile, it can properly be assumed that the bacteriemia had resulted from the joint infection. If the bacteriemia does not disappear following the adequate drainage of the joint, the presence of an associated bone infection must be assumed. The presumption is stronger if the inciting organism of the joint infection is proved to be a staphylococcus. Exploration of the contiguous bone is then indicated. In the average joint it sometimes becomes a matter of difficulty to locate the bone focus, or to decide which of the bones entering into the joint structure is to be explored, although commonly the presence of localized tenderness is an efficient guide. Should a competent focus be found and removed surgically and should this be followed by a disappearance of the bacteriemia, it can again be properly assumed that the latter resulted from the focus of osteomyelitis. When the bacteriemia still persists and the surgeon is certain that the bone lesion has been so thoroughly removed as to be apparently impossible of causing the bacteriemia and when the appearances of the bone wound corroborates this impression, the bacteriemia should be used as an indication that some other focus exists which must be found and removed in order to render the blood sterile. Many times this proves to be the case; but when it does not, the original focus of osteomyelitis should be examined again and revised operatively. If the bacteriemia still persists and the number of demonstrable bacteria is still comparatively small, an explanation of the bacteriemia becomes impossible for the moment, although it must necessarily be assumed that some other focus does exist which is causing the blood infection, and which for the moment is not demonstrable. Undoubtedly in some cases an obscure primary lesion exists which serves to keep up the bacteriemia. Fortunately, in most of such cases the natural forces of the body are ample after a sufficient elapse of time to render the blood sterile. A bacterial endocarditis must be excluded in all such cases.

If the inciting bacterium of the joint infection is a streptococcus and the patient is in the appropriate age, an epiphysitis is to be looked for; doubtless the operating surgeon will have demonstrated this lesion in exploring the joint and in establishing competent drainage. In order to conserve the normal growth of the bone at the given epiphyseal line, total or partial removal of the epiphyseal lesion is not advised and it is better surgery to allow nature to sequestrate that which has already been destroyed by the infection. Under these conditions, the bacteriemia will persist; usually, however, the natural protective forces of the body are sufficient eventually to render the blood sterile. If the grade of the bacteriemia should, however, increase to the dangerous point, further radical surgical measures become imperative.

In the presence of a pneumococcus infection, it is most exceptional for bone involvement to be present. Bacteriemias are not common, and are usually due to another lesion in the body at a distance from the joint infection. Conservative treatment of the joint is indicated.

2. When foci of infection coexist in more than one joint in the presence of a bacteriemia, the explanation of the latter becomes a matter of exclusion. Similar rules to those outlined in the last paragraph apply.

3. In a few of the cases, comparatively speaking, the primary lesion is demonstrable as well as one or more subsidiary lesions. In the majority of the cases, the primary bacteriemia disappears after efficient surgical treatment directed toward all the demonstrable lesions. In a few cases, however, the bacteriemia persists. Although in some of the latter cases, because of the character of the infecting organism or because of other reasons, it is possible to say with a fair degree of certainty that the primary lesion is keeping up the bacteriemia, in all of the others the proper explanation becomes a matter of exclusion also in accordance with the rules laid down.

4. In some of the cases of joint infection with bacteriemia a complication develops which is apparently unrelated to the arthritis. Except in those cases in which the complicating lesion is known from previous experience to cause a bacteriemia or general blood infection, the proper explanation again becomes a matter of exclusion as previously indicated. In any of these groups it is important to know the relative quantitative degree of the blood infection by an estimation of the number of organisms per cubic centimeter of blood (plate culture method). Then a comparison of any one blood examination either with preceding blood cultures or with subsequent ones readily gives a method of distinguishing whether improvement is or is not occurring.

5. Any of the local conditions indicated in the preceding four groups may be associated with a general blood infection in which the blood cultivations show that large numbers of viable organisms are circulating in the blood. It is to be assumed under such conditions that the bacteria

are multiplying in the blood in addition to whatever else they are doing; the prognosis must therefore be a serious one. The local lesion, or lesions, becomes a matter of least importance. The usual course of affairs includes a steady progression of the general blood infection until a fatality occurs. Exceptionally, improvement occurs and the patients recover. Some patients are admitted to the hospital when the general blood infection has already reached an extreme degree, that is, in a high grade of sepsis; such patients should not be operated on for any of their local lesions as they invariably die within a short time.

Patients in the first four groups of this classification may, at any time, as has been indicated previously, pass into group 5. They then assume characteristics of this group and the clinical manifestations increase in gravity proportionately and absolutely. It is rare for the opposite course to be followed.

In the group of joint infections with and without osteomyelitis and with bacteriemia, the disappearance of viable bacteria from the blood stream, as demonstrated by the blood cultivations, is many times due to the mechanical operative removal of the part of tissue carrying the infected embolus-thrombus formation. In epiphyseal lesions, mechanical removal of the focus of infection is not done; the disappearance of any accompanying bacteriemia must then, necessarily, be accomplished by the natural antibacterial agencies of the body. In others, the disappearance of the bacteriemia is a sudden thing due to the extrusion of the infected clot into the wound surface, or to other nondemonstrable cause of generally similar nature, or to the control of the infection by the relatively strong natural resisting powers of the patient. In still other cases, the bacteriemia becomes a more chronic affair and persists for some time before finally disappearing; anatomically this must be due to a slow healing of the lesion and the isolation of the infected clot by dense scar tissue, or, functionally, by the slow sterilization of the infected environment by the natural forces of the body.

A REVIEW OF UROLOGIC SURGERY

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(Concluded from page 773)

TESTIS AND VAS DEFERENS

Tumors of the Testis.—Keyes⁴⁴ states that a high mortality rate accompanies the treatment of malignant tumors of the testis by orchidectomy only. It is emphasized that for more successful treatment earlier diagnosis and more extensive operation or treatment by radiant energy must be made. Five conditions must be considered in the differential diagnosis: syphilis, hematocele, hydrocele, tuberculosis and cryptorchidism. Gibson and Kutzmann in their radical operations found that in only 50 per cent of cases could all malignant nodes be removed. Colley reported seventy-eight cases treated with serum; only twenty-two patients survived more than four years.

Keyes reports a case in which there was marked emaciation, a large testicular tumor, and extensive secondary masses in the abdomen. Orchidectomy was performed one week after treatment with radium packs. The abdominal masses subsided in several weeks, and ten years later the patient was living and well. Dean reported sixty-three cases in which treatment was carried out by radiation of low voltage to the testis and high voltage to the abdomen before orchidectomy. High voltage irradiation was repeated two months after the first treatment, orchidectomy having been performed in the meantime. Twenty-six patients (41 per cent) survived, six were well more than three years, and two more than five years. Thirty-nine cases were termed "recurrent inoperable," the patients having developed inoperable local recurrence or inoperable metastasis. Of these, eight (20 per cent) survived from six months to seven years after the first irradiation, showing that this treat-

44. Keyes, E. L.: Malignant Tumors of the Testicle; Diagnosis, Prognosis and Treatment, *Am. J. Roentgenol.* 15:44-49 (Jan.) 1926.

ment has at least arrested the disease. Following irradiation and orchidectomy 20 per cent remained well, in contrast to almost complete failure following simple orchidectomy with irradiation. It is pointed out that comparison is difficult between surgery and radiotherapy, since the latter begins where the former ends.

[Ed. NOTE.—The surgical removal of a primary malignant tumor with its metastatic growths is fundamental, depending primarily on an early accurate diagnosis, and also on complete permanent removal of the tumor. Applications of these principles in treating malignant conditions has markedly lowered the mortality rate. Diseases of the mouth, breast, uterus and testis are examples, and the fact that metastasis in these conditions occurs primarily along the draining lymphatics, which are surgically removable, still makes possible a small percentage of cures even in the later stages of the disease. Bloodgood has found, in thirty years' experience, that cancer of the tongue, when treated in the early stages, yields a cure in 62 per cent of cases, while only 12 per cent are relieved in the later stages. Hinman, in his radical operation of removing the lymphatic drainage of the testis, has raised the possibility of cure from 15 to 30 per cent in teratoma testis.

The advent of modern efficient radiotherapy tends to modify treatment somewhat. The encouraging results noted in recurrent inoperable cases are instructive, but should not be nullifying in those cases that can be cured by complete surgical removal. Undoubtedly radiotherapy is the treatment of choice in those cases exhibiting palpable abdominal metastasis. Levin has stated that the highly specific action of radium on the testicular cells undoubtedly explains the remarkable beneficial effect on some malignant tumors of the testis. The rays tend to destroy the spermatogenic elements without apparent injury to other elements. It has accordingly been our experience that the beneficial effect has been only in the seminoma (embryonal carcinoma). This is due to the fact that this type of tumor is derived from the spermatoblasts and is therefore regarded as especially amenable to radiotherapy; the mixed type of tumor (teratoma) is not necessarily so susceptible. It is interesting to note that Chevassu, the originator of the modern radical operation for testicular tumor, uses radiotherapy over the abdomen in the seminoma type of testicular tumor with metastasis and reserves the radical operation for the teratoma or mixed tumor.]

Bell⁴⁵ states that the seminoma and teratoma groups constitute the greatest number of tumors of the testis. Seminoma arises from a proliferation of the cells of the seminiferous tubules in the same way that glandular carcinoma arises in other organs. These are usually noticed in the fourth decade and they grow more slowly than the teratoid

45. Bell, F. G.: Tumors of the Testicle: the Spermatocytoma Group, *Brit. J. Surg.* 13:282-301 (Oct.) 1925.

carcinoma. They present in the main a specific structure, which may be definitely related to the seminiferous cells but is subject to certain variations. The question occasionally arises as to whether a tumor is carcinomatous or sarcomatous. Carcinomatous features usually prevail, but it is common to find mixed histologic characters in the same tumor. This feature is probably related to the mesothelial origin of the seminal cells and to reversionary tendencies. Like most germinal cell tumors, the seminomas behave like carcinoma and spread by way of the lymphatics. Occasionally, however, spreading by way of the blood stream suggests sarcomatous characteristics.

Vasotomy.—Belfield⁴⁶ finds that three possible injuries may take place through vasotomy: (1) injection of the solution outside instead of within the vas; (2) epididymitis, and (3) occlusion of the vas.

Extravasal instead of intravasal injection is possible through either of two errors: failure to distinguish the sheath from the vas or puncture of the vas by the sharp point of a needle after introduction into its lumen. Even the hypodermic steel needle whose point has been filed off may, after introduction, perforate the vas. For this reason Belfield has long used and recommended the blunt silver canaliculus needle.

Epididymitis does not, and probably cannot, result from the mechanical injury or from the effect of ordinary chemical solutions properly injected. Twenty-two years ago, before performing vasotomy on the patient, Belfield carried it out on dogs; when, contrary to his expectation, epididymitis did not occur, he injected mild silver protein solution toward the testis, and found it impossible to make this black liquid pass beyond the tail of the epididymis. In an experimental study Rolnick also proved, and by roentgenograms demonstrated, the impossibility of injecting beyond the tail of the epididymis of the dog. A similar demonstration has been made by Luys of Paris, in his study of vasotomy, and he has adopted this procedure in place of his earlier practice of injecting the vesicles through the ejaculatory ducts. In man he has never seen epididymitis caused by vasotomy. He has, however, seen epididymitis follow a pus infection of the vasotomy wound; this is, so far as he knows, the sole causative relation between vasotomy and epididymitis.

Occlusion of the vas is possible through extensive laceration of the vas, its sheath or adjacent tissues, which is of course needless in performing vasotomy. Occlusion may occur through the injection of chemicals that destroy the epithelium lining the vas, with subsequent union of the denuded surfaces. Of the many solutions used, many are the milder silver protein compounds, mild silver protein and neosilvol, in 10 per cent solution; the recent chlorine preparations, hyclorite, and chlorazene

46. Belfield, W. T.: Injuries Possible Through Vasotomy, *J. Urol.* 14:349-353 (Oct.) 1925.

1:200, are not known to destroy the epithelium of the vas. Of the newer mercurial bactericides, mercurochrome-220 soluble in .1 or 2 per cent solution is reported as harmless by some clinicians (Cumming, Ockerblad) although found to be harmful by others (Kile); Rolnick found a 2 or 3 per cent solution destructive to the epithelium of the vas in dogs. Possibly a weaker solution, 1:300 or 1:500, might prove both efficient and harmless.

Occlusion of the vas may be induced by infection of the wound, with subsequent cicatrix formation. An insidious cause of occlusion is the regurgitation, past the vesicle into the wound, of some substance which, while harmless to the lining, provokes in connective tissue a cicatricial formation by which the vas is compressed. Belfield has seen this only through the use of colloidal silver solution. To avert such regurgitation he has compressed the vas by a silkworm stitch, passed through both edges of the skin incision and under the sheath of the vas, leaving it in position for four days.

Thomas⁴⁷ differentiates vasopuncture and vasotomy or vasostomy. His technic of vasopuncture is as follows: The seminal vesicles are emptied of their inflammatory products as completely as possible by massage just prior to injection. A vertical incision of about 1 inch (2.5 cm.) is made in the skin and fascial sheaths, and the vas isolated and brought out of the wound on the curved flat end of a probe; or, preferably, the vas is encircled through its sheaths by the towel clips as soon as the skin is incised, facilitating its exposure, or it is cut directly down on. The fascial coverings are then stripped from the vas, which facilitates the introduction of the needle. A few cubic centimeters of sterile water is injected to determine the patency of the vas and ejaculatory ducts. The lost resistance as the needle enters the lumen of the vas, together with the visible ascent of a tiny black column in the axis of the vas after the injection of about 2 drops of colloidal silver, without resistance, inform the experienced operator that the needle is properly in the lumen and that there is no stricture of the vas. If for any reason the needle cannot be correctly introduced into the lumen of the vas, or if a stricture is found, the injection is not attempted, as a disagreeable vasitis, funiculitis and occlusion of the vas may result. In the absence of any mishap or obstruction, the syringe is filled, preferably with 3 to 5 per cent solution of one of the silver protein preparations, or perhaps 0.25 per cent chlorazine, and the quantity slowly injected. As the needle is withdrawn pressure by gauze prevents reflux, and subsequent regurgitation and extravasation into the spermatic cord are prevented by the introduction of a fine plain catgut suture through the external

47. Thomas, B. A.: Vasopuncture, a Technical Modification of Vasotomy for Seminal Vesiculitis, *J. Urol.* 14:331-347 (Oct.) 1925.

coat of the vas. Herein rests the superiority of vasopuncture over vasotomy, as the operator is better able to control regurgitation from the vas and its attendant disastrous consequences; in vasotomy such perfect control does not exist, and there is more traumatism and greater proclivity to infection and formation of stricture.

Mark⁴⁸ states that whether drainage of infected vesicles is established through the normal point of discharge as provided by nature, or by opening the sac through some other point of selection, must depend on the judgment of the surgeon based on the degree of pathologic change. It is equally as axiomatic that when the infection has invaded the walls of the sac to the degree that drainage will not suffice, and when the removal of the sac is not incompatible with life, such removal is indicated and justifiable if the restoration to health of the patient demands it. Further, it is recognized that the treatment of an infected sac by bactericidal agents without drainage avails nothing and is essentially poor surgery. Mark concludes that vasotomy is indicated only when this operation facilitates or establishes drainage. Horsley has shown that when a foreign substance is introduced into a cavity lined with epithelium, two forces are set at work for its expulsion and protective drainage, spasmodic efforts on the part of the surrounding musculature and a reversal of the lymph stream. He believes that too much stress cannot be laid on these physiologic factors in considering the good effects that may be secured from vasotomy.

Wesson⁴⁹ reports a series of forty-seven cases of vasitis; the majority of these cases had been referred to him by insurance men for examination with the statement that operation for hernia had been advised. These cases had been diagnosed because of the history of pain in the groin following a strain, and the presence of bubonocoele or thickened tender spermatic cord, which interfered with accurate palpation of the inguinal rings. Urine was found infected in eighteen cases; residual urine, secondary to median bars in four; pus in the prostate and seminal vesicles in forty-seven; tender thickened vas in forty-seven; chronic epididymitis in thirty, and genital tuberculosis in three.

CARCINOMA OF THE PENIS

Dean⁵⁰ reports his results in the use of radiotherapy in sixty-one cases of carcinoma of the penis. The following groups are considered:

1. Six cases in which there was a superficial local lesion without metastasis. Five of these patients were living and well from one year to five

48. Mark, E. G.: Indications for Vasotomy, *J. Urol.* 14:323-330 (Oct.) 1925.

49. Wesson, M. B.: Industrial Hernia Versus Seminal Vesiculitis and Vasitis, *California and West. Med.* 24:212-217 (Feb.) 1926.

50. Dean, A. L., Jr.: The Treatment of Epithelioma of the Penis with Radium and Roentgen Rays, *Am. J. Roentgenol.* 15:36-43 (Jan.) 1926.

years and eight months after irradiation. 2. Thirty cases in which there was extensive local tumor without metastasis. Twenty-one of these patients were living and well, seven from three months to one year, three from one year to two years, three from two to three years, two from three to four years, and six from four to five years; five were known to have died, and four were lost from the records. 3. Sixteen cases in which there was extensive local tumor and metastasis to the groin. Four of these patients were living and well from one year to three years and seven months after irradiation; seven were known to have died, and five were lost from the records. 4. Eight cases of post-operative recurrence; three of these patients were known to be living and well from four years to five years and three months later; three were known to have died, and two were lost from the records. 5. One case in which irradiation was carried out postoperatively as a prophylaxis against recurrence. This patient was living three years and two months later; there had been metastatic growth in the groin which was removed at operation.

Dean concludes that in the treatment of primary epithelioma of the penis and metastasis the element of infection must be eliminated as soon as possible; that a superficial epithelioma should undergo complete regression when treated with a surface applicator of radium emanation, 65 millicurie hours for each square centimeter, filtered through 0.5 mm. of silver, and that if the tumor has invaded the cavernous tissues the treatment of choice is thorough irradiation followed by conservative amputation. Surface application of radium emanations is preferred, as it is less traumatizing and more convenient. In some cases inguinal metastasis disappears after irradiation with the roentgen rays. If after such treatment the metastatic nodules do not steadily decrease in size, firmness and degree of fixation, and the cause of delay cannot be ascribed to infection, careful resection is in order. The high voltage roentgen-ray irradiation is more efficient than that delivered by the low voltage machine for the treatment of metastatic nodules of all depths. When high voltage roentgen-ray machines are available it is unnecessary to depend on the radium pack for deep application.

URETHRA

Diverticulum.—According to Verriotis and Defrise,⁵¹ cases of urethral diverticula of congenital origin in women are rare. The most frequent causes of acquired diverticula are trauma during delivery, direct trauma, inflammatory conditions or the opening from inside the urethra of cystic cavities of the urethrovaginal septum. These conditions usually

51. Verriotis, T., and Defrise, A.: Des diverticules urétraux chez la femme, J. d'urol. 21:97-122 (Feb.) 1926.

suggest disease either of the genital system or of some other portion of the urinary tract. There is usually more or less infection of the diverticular pouch. The diagnosis is definitely determined by urethroscopic or roentgenographic examination. Radical operation gives the best results; it consists in resection of the diverticular pouch and in the urethrovaginal plastic operation. Without surgical treatment the condition rarely improves.

Young and Shaw⁵² classify urethral diverticula as congenital and acquired. The latter arise (1) from dilatation of the urethra due to urethral calculus or urethral stricture, and (2) with perforation of the urethra resulting from injuries to the urethra, rupture of abscesses into the urethra, and rupture of cysts into the urethra. A report is given of a case of diverticulum following perineal prostatectomy. The diverticulum was completely excised. The division was made at the connection with the prostatic urethra. The urethral opening was closed with mattress sutures of plain catgut. Sutures were used to tighten the external sphincter. An inverted skin incision was made in the line of the wound made for the old prostatectomy. The sac was easily exposed without opening and followed downward into the depths of the perineum. It was about 1 inch (2.5 cm.) in diameter externally and had a gradually narrowing gourdlike neck, which in its deeper portions was about 5 mm. in diameter externally. The neck of the sac was followed to its juncture with the urethra at the apex of the prostate, where it was excised. The connection was only 2 or 3 mm. in diameter. The mucous membrane was then turned in with a pursestring suture of plain catgut. Examination of muscles in the region of the triangular ligament and external sphincter showed definite impairment. There was no recurrence of the diverticulum after operation; there was moderate incontinence, usually during the day.

Duplication.—Fronstein and Saïgràjeff⁵³ state that anomalies of the urinary and sexual organs occur frequently on account of the fusion of these organs in embryonic development. In 148 anomalous cases of such type, eight cases of duplication of the urethra were noted. Double urethra, beginning at the external orifice and belonging to the pendulous portion of the urethra, is rare, and a double urethra extending to the bladder is unusual.

Of four cases described by Fronstein and Saïgràjeff, one involved the posterior urethra and the posterior portion of the pars pendula penis. In the first case described there was an accessory urethra, 15 cm. in

52. Young, H. H., and Shaw, E. C.: Urethral Diverticula, *South. M. J.* 19: 42-45 (Jan.) 1926.

53. Fronstein, R. M., and Saïgràjeff, M. A.: Zur Frage der Duplikatur der Harnröhre, *Ztschr. f. urol. Chir.* 17:187-204, 1925.

length, lying dorsally and extending from the outer opening of the urethra to the prevesical tissues, but no connection with the bladder or the true urethra was noted. A histologic structure similar to the true urethra was noted. Resection was carried out because of infection. A good result was obtained. In a second case two parallel channels occupied the anterior portion of the penile urethra. The dorsal channel connected with the lower one 6 cm. from the meatus. A third patient presented a dorsal blind canal leading 3.5 cm. backward and separated from the lower canal by a thin membrane. The fourth case is remarkable in that none other like it can be found on record. The accessory channel found at necropsy extended from the bladder to the peripheral third of the pendulous portion of the urethra. It contained the openings of the ejaculatory ducts and the colliculus seminalis. It passed through the prostate parallel to the true urethra, which was markedly constricted. Farther forward the accessory channel became dilated and continued to the end of the penis.

The authors review the literature on urethral duplication and seek to show that the condition is caused by embryonic maldevelopment of entoderm and ectoderm of the sinus urogenitalis. When possible radical extirpation of the accessory channel is the treatment recommended.

[ED. NOTE.—The urologist, perhaps as frequently as any specialist, is called on to consider anomalous development of the structures with which he deals. To trace the embryogenetic relationships of the parts involved in such malformations affords unusual opportunity for detailed anatomic study, both from the standpoint of understanding the individual anomalous structure and from the more practical point of view as to how best to apply plastic surgery in reconstructing the parts for proper function. In the case of duplication of the urethra the foregoing article is timely, as Fronstein and Saigràjeff carefully explain the different types encountered, the lesions that are likely to arise in consequence, and the technic for handling the individual case to best advantage.]

Stricture.—Huddy,⁵⁴ in a review of the subject of internal urethrotomy, reports the study of 109 operations on 107 patients. The main types of stricture which require urethrotomy are: (1) the narrow type, which is permeable with considerable difficulty and in spite of repeated efforts will not dilate readily; (2) the resilient type, which dilates but as readily contracts, and (3) the type in which perineal fistula is associated, provided the fistula persists solely because of the presence of a stricture in front of it and not on account of a chronic infective condition.

Operation is contraindicated in cases in which the stricture is impermeable. The operation should be preceded by suprapubic drainage of

54. Huddy, G. P. B.: Some Considerations of the Operation of Internal Urethrotomy and the End-Results Thereof, *Brit. J. Surg.* **13**:458-465 (Jan.) 1926.

the bladder if there is evidence of renal insufficiency or marked urinary infection. A periurethral abscess should first be drained and internal urethrotomy performed when the infection has subsided. Urinary extravasation is best treated by free incision into the infected parts combined with perineal drainage of the bladder, internal urethrotomy being performed at a subsequent operation.

The results are extremely satisfactory, and the operation should be carried out in any case if dilatation is difficult or unsatisfactory. An indwelling catheter for drainage is beneficial and should, unless some complication arises, remain in position four days. Postoperative dilatation is essential.

Chauvin⁵⁵ reported a case of ruptured urethra before the Surgical Society of Marseilles.

The patient fell astride a piece of iron. Swelling of the scrotum, hematuria, dysuria and fever occurred. Later there was retention of urine, the penis became edematous and gangrenous, and cystostomy was performed as a preliminary procedure. The perineum was incised with the evacuation of foul-smelling pus. The necrotic tissue was removed and the urethra was opened for a distance of about 3 cm. Three weeks later, when all infection had ceased, the urethra was again explored. It was almost completely closed from 2 cm. behind the meatus to the perineum; the obstruction or stricture was not ring-like as is usual, but was apparently continuous along its length. Only a filiform could be passed. A complete urethrotomy the whole length of the penis was performed. This was followed by a methodical destruction of the hair of the neighboring areas. Later a urethroplasty following Escat's method was done; the new urethra was made with continuous flaps and overlying grafts, for which a portion of the prepuce and a piece of the scrotum was used. In about three weeks a no. 21 catheter could be passed easily, and the canal showed no further tendency to stricture.

An interesting point of jurisprudence is brought up: This man had a gonorrheal stricture before the trauma. It seems logical that the trauma would have been much less severe if it had not been for the presence of the old gonorrheal stricture. The bursting of the urethra occurred in an area of dilatation behind the stricture.

Cecil⁵⁶ reports a case of a girl, aged 11, with diurnal and nocturnal incontinence. When the child was 4 years old, she had had a severe pain in the region of the bladder which lasted for several months. Eight months later, she passed a large stone, about 3 by 1.5 cm. Following this incontinence developed. The general examination was negative. It was noted on attempting to examine the genitalia that the child habitually kept the thighs firmly adducted, and when told to walk she was inclined to walk with as little motion

55. Chauvin, E.: Rupture traumatique d'un urethra retreci: Uretroplastie sur une longueur de 10½ cm., *Arch. franco-belges de chir.* 28:720-723, 1925.

56. Cecil, A. B.: Destructive Lesions of the Female Urethra in Childhood: A Differential Diagnosis from Female Hypospadias, *J. Urol.* 14:441-475 (Nov.) 1925.

of the thighs as possible; she even ran in this manner. Urine constantly dripped from the vulva, both when she was lying down and when she was walking, and the skin surrounding the vulva was excoriated. The labia were held firmly together. The clitoris and labia minora were normal, but there was no evidence of a hymen. The external urethral orifice appeared normal and was in a normal position anteriorly. A soft rubber catheter introduced into this orifice appeared in the vagina, and it was found that the urethra extended back for 1.5 cm. from the external urethral orifice. The urethra easily permitted the passage of a no. 14 catheter. For about 1 cm. the urethra was of normal thickness, but near the vaginal portion it became thinner and almost weblike. The inner portion of the urethra extended from the anterior vaginal wall. At this point its edges were excoriated, and urine salt was adhering to it. Back of this anterior portion of the urethra there was nothing to indicate the urethra except a change in color of a strip of the anterior vaginal wall. There were no lateral walls, nor any tags, nor evidence of scar. With the aid of a speculum, a round opening in the wall of the bladder directly into the vagina was found. The edges of the opening were thin and it was without power to retain urine, remaining constantly open; the whitish bladder wall could be seen flapping against it. The index finger was easily introduced into the vagina. Just above the internal urethral orifice was a constriction which would not permit the easy passage of the finger, and no further attempt was made to do so. By two operations a urethra was constructed which functioned satisfactorily.

Calculi.—Lempert⁵⁷ reports a case of urethral stones in a man, aged 38. The roentgen ray revealed an irregular shadow of a stone, about 2 by 4 cm., in the perineal area. Under local anesthesia, the posterior urethra was split a distance of 2 cm. Eleven stones were removed; the largest was about 7 cm. in diameter. Three of the stones were faceted. The entire group of stones weighed 9.3 Gm., and measured 4.1 cc. by volume.

ANESTHESIA

Papin⁵⁸ has employed ethylene gas anesthesia in most of his urologic operations for the last two years; he rarely uses local, regional or spinal anesthesia. A perfect anesthetic must be one that is effective but harmless. Ethylene was found to be much more effective than nitrous oxide, which he had been using for two years. He began using it in animal experimentation and then he used it in man in 700 cases, and found that it presents no disadvantages. Mixed with oxygen, ethylene is administered like nitrous oxide, but correct induction requires experience. Before giving ethylene a subcutaneous injection of pantopon is given to quiet the patient. Anesthesia is complete in from one to twelve minutes, the average being five minutes. Recovery as a rule is quick,

57. Lempert, Fritz: Harnröhrensteine, Zentralbl. f. Chir. 53:214-215 (Jan. 23) 1926.

58. Papin, E.: Anesthésie à l'éthylène, XXV Cong. Franç. d'Urol., Presse méd. 2:1446, 1925.

and there is no vomiting or excitation. Ethylene does not affect the functioning of the kidneys. Patients with nephritis, serious pulmonary and cardiac lesions were operated on successfully.

Papin states that ethylene gas is highly inflammable and when mixed with oxygen explodes with a loud report on coming in contact with a flame, but if the same precautions are taken as with ether, accidents are avoided. Aside from its inflammability, Papin regards ethylene as the best anesthetic in urologic cases.

[ED. NOTE.—Ethylene gas is particularly desirable as an anesthetic for urologic surgery. The surgeon finds it most necessary to conserve the remaining function of the kidneys. Dealing as he usually does with aged patients, many of whom have renal lesions, any anesthetic that does not add to the postoperative strain on the kidneys is a desirable asset. According to investigators who have used ethylene in a large number of cases, it does not differ from nitrous oxide in its degree of inflammability. The occasional explosive accidents have had wide publicity. The usual precautions necessary for the safe conduction of a nitrous oxide-oxygen anesthesia are generally also sufficient for ethylene anesthesia. Various methods for preventing static spark explosion have been devised; the simple grounding of the operating table to the floor drain pipe is usually sufficient to guard against this possible igniting factor.]

Shaw⁵⁹ reports a study of experimental and clinical data on epidural anesthesia in perineal prostatectomy. Extradural injections of various quantities of methylene blue solution were made in eleven fresh cadavers in an effort to determine the upward extension of solutions injected through the sacral hiatus. It was found that from 15 to 20 cc. completely filled the extradural space in the sacral canal, and that solution in excess of this quantity extended into the thoracic and lumbar regions of the vertebral canal.

A series of 100 cases of perineal prostatectomy performed under extradural nerve block anesthesia are described. Transsacral injections and local infiltration were not employed. The dosage and concentration of the anesthetizing solution underwent variation from time to time, while attempts were made to find the most satisfactory method of producing complete anesthesia with the minimal unfavorable reaction.

Among the 100 cases complete anesthetization failed in 17 per cent. If patients had definite pain the anesthetics were classified as failures, even though the operation was completed without a general anesthetic. A general anesthetic was given in eleven cases.

59. Shaw, E. C.: Epidural Anesthesia for Perineal Prostatectomy: An Experimental and Clinical Study, with Report of 100 Consecutive Cases, *J. Urol.* 15:219-265 (March) 1926.

The incidence of satisfactory anesthesia was not proportional to the amount of procaine solution used, but was proportional to the concentration of the solution. The best results were obtained with from 15 to 20 cc. of 3 per cent procaine. The percentage of failure was not only reduced, but the anesthesia was more complete.

Blood pressure determinations, as well as pulse and respiration rates, were made in all cases at five minute intervals from the time of injection to the completion of the operation. The blood pressure was found to be the best indication of the patient's condition. The systolic blood pressure frequently fell from 30 to 50 mm. with no change in the patient's appearance.

Two distinct types of reaction were observed. One consisted of increase in blood pressure and pulse rate, and in excitability and convulsive movements, apparently due to general procaine intoxication resulting from absorption of the drug into the blood stream. This type was rare, being observed in only two cases. The second type consisted in decrease in blood pressure, slowing of the pulse rate and extreme weakness, occurred much more frequently, and was probably due to the localized paralytic action of the excessive amount of solution on the sympathetic nerves making their exit from the cord in the thoracic and upper lumbar segments. Practically no reaction occurred if the patients received from 15 to 20 cc. of 3 per cent procaine.

The ultimate mortality rate in the 100 cases was 3 per cent. None of the deaths was attributable to the anesthetic.

Extradural anesthesia produces complete relaxation of the muscles of the perineum, thereby facilitating the operation. The postoperative complications are definitely less than those following any type of general anesthesia. Postoperative pneumonia and uremia did not occur. There was only one case in which cardiac decompensation developed. This was mild and the patient recovered. Supplementing extradural block with transsacral injection is unnecessary.

Epidural anesthesia should not be used in nervous uncooperative patients unless general anesthesia is definitely contraindicated. Among younger patients in good general condition, the choice of an anesthetic is of no great importance, but among old, debilitated patients with impaired renal function, extradural anesthesia undoubtedly reduces the operative risk.

[ED. NOTE.—Shaw states that it is not necessary to supplement the extradural block with transsacral injections; he reports 17 per cent of failures. In a recent report by Meeker and Scholl, 270 cases of prostatectomy under transsacral anesthesia are reported with only 5.8 per cent of failures. In a large series of cases it was found that simple epidural injections were unreliable and resulted in failure too frequently.

The transsacral blocking is more difficult and requires more time for injection, but the patient is ready for operation immediately after administration of the anesthetic without the delay necessary following the single caudal injection.

In a series of more than 1,800 cases, Meeker and Scholl⁶⁰ found a 1 per cent solution to be the most satisfactory. In a series of 500 cases, mostly simple caudal injections, the strength of the solution was from 2 to 3 per cent; in these cases reactions were much more common and the anesthesia was not as satisfactory as when a 1 per cent solution was employed.

Regardless of the technic of the method employed, the introduction of sacral anesthesia has unquestionably been a factor in the lowering of the operative mortality rate following prostatectomy. The operative mortality rate in cases in which sacral anesthesia was employed is less than half that following prostatectomy under either ether or spinal anesthetics. In patients recovering from operation, there was no difference in the late results following the different types of anesthetics. Sacral anesthesia does not entirely eliminate the possibility of respiratory infection; when this occurs following the administration of ether it is usually attributed to pulmonary irritation from the anesthetic. Sacral anesthesia definitely eliminates the group of immediate deaths usually attributed to shock and cardiac disease.]

Bilger⁶¹ reports a series of cases of epidural anesthesia used in Marion's urologic service. It was successful in seventeen cases, partially successful in two, and a failure in six. No accidents were noticed, although one patient had a slight collapse, and another had a marked sensation of cold in the lower extremities followed by intense trembling. Some inconveniences may be encountered in the obese patient, as the landmarks may be difficult to find. Anatomic anomalies, such as an exaggerated curvature of the sacrum, ossification of the membrane or narrowness of the sacrococcygeal hiatus may be present. Sacral nerve blocking is of definite benefit when a general anesthetic cannot be used, for old people and for patients with arteriosclerosis and pulmonary, cardiac or cardiorenal disease. There is less danger than with spinal anesthesia; it lasts at least two hours and there is no postoperative pain. This method of anesthesia is especially indicated in all operations on the urethra and in the bladder, except litholapaxy. In ten patients with prostatic disease operated on by Marion, definite success followed in only five. The prostate sometimes remains sensitive. Should the

60. Meeker, W. R., and Scholl, A. J.: Sacral Nerve Block Anesthesia, *Ann. Surg.* 80:739-772 (Nov.) 1924.

61. Bilger, F.: De l'anesthésie épidurale en chirurgie urinaire, *J. d'urol.* 19:111-126 (Feb.) 1925.

anesthesia be perfect, other disadvantages may present themselves: (1) It may be necessary to make a separate field block for the skin; (2) the rigidity of the abdominal muscles may prevent satisfactory exposure; (3) enucleation of small and hard nodules may provoke a painful pulling sensation of the peritoneum, which is nevertheless bearable, and (4) the nervous state of the patient may be an obstacle to the good results.

UROGRAPHY

Braasch⁶² reviews the difficulties arising from the interpretation of pyelograms. He states that correct interpretation of a pyelogram is based on familiarity with the outline of the normal pelvis. Unless one is thoroughly familiar with the possible variations in the outline of the normal pelvis, it is difficult to recognize deformity.

Incomplete filling of the pelvis and calices is a frequent source of error in interpretation. Unless the outline is complete, the apparent deformity may be taken for neoplasm or cortical necrosis. On the other hand, as the result of insufficient distention, hydronephrosis, anomaly and other lesions may easily be overlooked. Certain renal pelves are particularly difficult to outline, as repeated attempts may show. There is a marked difference in the rapidity with which the pelvis empties itself following distention with the pyelographic medium. If the pelvis is spastic a pyelogram made a short time after distention will usually show only a partially outlined pelvis, whereas in other types the medium may be retained and may outline the entire pelvis for several minutes after the injection. Blood clots may cause apparent filling defects in the outline, which are suggestive of neoplasm or soft stone. Postoperative deformity such as results from removal of stones, fixation of a kidney, drainage and exploration is often confusing.

Correct interpretation of the outline of the ureter is particularly difficult, and the personal equation is important. Irregularities in the outline of the ureter have been variously interpreted, and the diagnosis of stricture, kinks and pathologic irregularities has been made with comparatively little accurate basis for such interpretation. The elasticity and distensibility of the ureter is not generally recognized. Areas of apparent dilatation are readily outlined in the normal ureterogram as a result of localized areas of overdistention. On the other hand, the ureter may actually be dilated, and when incompletely filled gives a similar appearance. Complete uniform distention of the ureter is essential to correct interpretation, as in the renal pelvis. This, however, may be difficult, and although a number of suggestions have been made with regard to methods of securing uniform distention, they are not always

62. Braasch, W. F.: Errors in the Interpretation of Urographic Findings, *I. Urol.* 14:631-639 (Dec.) 1925.

